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Vol 20, No 3, May-June 1986

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SPACE BIOLOGY AND MEDICINE ON THE TWENTY-FIFTH ANNIVERSARY OF THE FIRST SPACEFLIGHT OF YURIY ALEKSEYEVICH GAGARIN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 27 Jan 86) pp 4-12

[Article by O. G. Gazenko, N. N. Gurovskiy and A. A. Gyurdzhian]

[Text] Cosmonautics has come a very long way in the quarter century that has elapsed after the hisotrical day of the flight of Yu. A. Gagarin on 12 April 1961. The first flight, which lasted only 108 min, was to determine human capacities as an operator under conditions prevailing in space.

Yu. A. Gagarin had only a few sheets of paper, on which he was able to write his sensations and impressions. In contemporary flights, our cosmonauts work with a very large number of documents and logs, in which they record the progress and results of numerous investigations that they conduct in the interests of basic and applied sciences, as well as for many sectors of the national economy. And they use the most diverse and refined instruments and tools.

As of 1 January 1986, Soviet cosmonauts had made 109 manned flights involving 60 people. Some of the participants had been in space 2-3 and even 5 times (V. A. Dzhanibekov). The Salyut orbital stations became a permanent space research laboratory. The crew consisting of L. D. Kizim, V. A. Solovyev and O. Yu. Atkov worked in space for 237 days. V. A. Dzhanibekov and V. P. Savinykh were able to "find" and dock with the inactive Salyut-7 station in space, repair it and completely restore its work capacity.

In the 25 years that have passed since the first flight, cosmonautics has become a solid part of our life, an inseparable element of scientific, economic and sociocultural life of mankind. The file of organizations that are planning spaceflights is full of applications for investigations in the interests of the most diverse scientific disciplines and the national economy.

To what can we attribute such rapid development of cosmonautics and its swift intrusion into our life? The answer is rather simple. Man's breakthrough into space was not a chance phenomenon, the achievement of some single branch of knowledge or a group of branches. It was the logical outcome and necessary link in the entire history of civilization, development of science, engineering,

economics and culture of human society. On the other hand, man's penetration into space is not only the logical outcome, but the turning point in the history of mankind, which has and will have in the future a stimulating and revolutionizing influence on progress of science, engineering, economy and culture. Paul Campbell, one of the pioneers in aerospace medicine in the United States, wrote well about this as far back as 1965 in his book, "Earthman, Spaceman, Universal Man." [Translator's note: Russian title is "Man-Cosmonaut--Citizen of the Universe"]. Some scientists compare the impact on mankind of penetration into space to the role in biological evolution of the exit of living organisms from the marine habitat to land.

The world will always be grateful for the feat of the Soviet people and Soviet cosmonaut, Yuriy Alekseyevich Gagarin, who pave the road into space for mankind. One of the American cosmonauts acknowledged this: "We all entered space through the door that was opened to us by Yuriy Gagarin."

Medicine became immediately involved in space research. Not even a month had gone by after the launch of earth's first artificial satellite on 4 October 1957, and already the first orbital biological experiment with the dog, Layka, aboard the second artificial earth satellite was performed on 3 November of the same year. Then, in 1960-1961, in the period preceding manned flight, a series of biological experiments was performed aboard satellite spacecraft that were returned to earth. The studies were conducted on dogs, other animals and many biological objects on different levels and lines of evolutionary development. This is how systems for life support, safe flight and return to earth were developed, as well as methods of screening and preparing living beings for flight, medical monitoring and recording physiological functions, and subsequent observation and analysis of findings. The experiments demonstrated the feasibility and safety of manned spaceflights. However, the importance of these experiments is not limited to biological exploration of space. They laid the foundation for a new branch of knowledge, space biology and medicine.

Biological experiments in space were continued thereafter--on dogs (Veterok, Ugolek), monkeys and various biological objects flown aboard satellites of the Cosmos series, when it was necessary to perform a physiological analysis of problems that arose. However, problems of human work capacity in flight, man's adaptation to flight conditions, work and rest schedules, protection against adverse factors, preparation and training, medical monitoring and examination in flight, postflight observation and rehabilitation, as well as space ergonomic and engineering psychology, could only be solved in manned flights with the participation of cosmonauts.

It should be noted that medicine continued to keep up with space research at the pace set by representatives of engineering and other concerned disciplines; it provided ongoing solutions for biomedical problems that arose. The USSR State Prize was bestowed upon a number of specialists for their successful work on such problems.

However, space medicine was not limited solely to medical support of missions. Using the unique opportunities offered in connection with investigation of new factors, conditions and approaches, it gained deeper knowledge of the

fundamental bases of biology and medicine, it enriched clinical medicine with new methodological procedures, criteria and valuable observations.

We should dwell on some factors and conditions that were instrumental in the efficient and successful involvement of medicine in space research. One of these factors was the solid theoretical foundation of our biological and medical science, based on the progressive teaching and principles of classics in science of our country: V. I. Vernadskiy, I. P. Pavlov, L. A. Orbeli and many others. As far back as 1934, at a conference dealing with investigation of the stratosphere, L. A. Orbeli along with other specialists formulated the basic biological and medical problems of exploration of the top layers of the atmosphere and space, whereas in 1935 an experiment was performed with Drosophila flies that were flowing aboard the USSR-1-bis stratostat to an altitude of 15,900 m. The second factor was the successful development in the USSR of aviation and rocketry, which drew the attention of biologists and medical specialists. Collaboration with specialists in aerospace engineering turned out to be extremely beneficial to biology and medicine, since enrichment of their armamentarium with methodological procedures, apparatus and engineering knowledge provided for the link with practice that makes it possible to work in step with technological progress, to see and test in practice the accuracy of theoretical constructions. The third factor is the methodological armamentarium and experience gained by aviation medicine, which made it possible, already in the early 1950's, to perform regular experiments with dogs on geophysical rockets climing to altitudes of 100, 200 and then 473 km. The fourth factor was the enthusiasm of laboratory associates.

The staff of the laboratory headed by V. I. Yazdovskiy included aviation physicians A. V. Pokrovskiy, A. D. Seryapin, O. G. Gazenko, Ye. M. Yuganov, A. M. Genin, I. S. Balakhovskiy and I. I. Kasyan, physiologists A. A. Gyurdzhian, A. R. Kotovskaya, V. S. Georgiyevskiy, S. F. Simpura and T. S. Lvova, and engineer B. G. Buylov. Their job was to make use of the knowhow of aviation medicine, as well as theoretical and methodological resources of physiological, medical and biological science, and to provide medical support for forthcoming biological experiments during spaceflights, thereby laying the foundation for man's first flight into space. The laboratory received much support in this work from well-known scientist-physiologists V. N. Chernigovskiy, V. V. Parin, A. V. Lebedinskiy, biologist N. M. Sisakyan and the academic scientific institutions which they headed. Much credit is due to Academician Norayr Martirosovich Sisakyan for the fact that the laboratory did not limit itself to medical support of future flights, but viewed in its work the captivating prospect of formation of a new branch of science, space biology and medicine, which was to have a positive impact subsequently on development of "earth" biology and medicine. In view of expansion of the work and impending tasks of screening and training cosmonauts, N. N. Gurovskiy and Ye. A. Karpov joined in the work of the laboratory.

Later on, the range of physiological, hygienic, general biological, clinical, psychological and other aspects included in space biology and medicine kept widening. More and more new specialists and various institutions became involved in the work (as members of regular staff and nonstaff associates).

Thus, many biomedical and sociopsychological disciplines made their contribution to the establishment of space biology and medicine. Among them, aviation medicine stood in first place, and space medicine was its direct offspring. Since that time, space biology and medicine is helping with its research in the development of branches of science that were involved in its formation. It offers them unique conditions for research, extremely valuable material, which opens up new prospects for investigations, interesting results that are the basis for important theoretical generalizations and new ideas. In view of the need to solve global problems of space biology and medicine, the Institute of Biomedical Problems, USSR Ministry of Health, was founded in November 1963.

By now, space biology and medicine is a completely formed independent discipline with its own theoretical foundation, its own methodology, its own system of concepts and terminology. Since 1962, Nauka Publishing House has been putting out the "Problemy kosmicheskoy biologii" [Problems of Space Biology] series (by now 55 volumes in this series have been published). The Meditsina Publishing House has been publishing the journal, KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA since 1967. Soviet scientists are regular participants at international congresses and symposiums dealing with cosmonautics, aviation and space medicine.

Representatives of virtually all medical disciplines, theoretical and clinical, as well as design engineers, psychologists, pedagogues and other specialists, are collaborating with space biology and medicine. They are enriching it with their methods and are directly involved in biomedical investigations. At the present time, we can already refer to space microbiology, immunology, toxicology, cardiology and gastroenterology. The list could go on and on. Thus, it can be stated that space biology and medicine are really included in the life of biomedical, sociopsychological and engineering-technical sciences.

Data referable, in particular, to science analysis, are indicative of the rate of growth in scientific interest in problems of space biology and medicine. The bibliographic guide, "Biomedical and Sociopsychological Problems of Spaceflights" ["Mediko-biologicheskiye i sotsialno-psikhologicheskiye problemy kosmicheskikh poletov"](Nauka Publishing House], listed already in the first 5 years (1961-1965) about 4700 sources, more than 8200 in the second 5 years (1966-1970) and about 10,000 in the third (1971-1975) (in spite of the stricter selection of references).

To date, three physician-cosmonauts have worked during spaceflights: B. B. Yegorov, V. G. Lazarev and O. Yu. Atkov. The latter performed an enormous program of medical investigations in the mission which lasted a record time of 237 days, and having analyzed and generalized the results with his colleagues, advanced an original conception of physiological adaptation (in particular, of the cardiovascular system) to weightlessness and the return to earth's gravity.

Here are some of the directions of investigations conducted by space biology and medicine:

General biological aspects. Only spaceflights have made it possible to study such problems as the effect of different levels of gravity (from weightlessness to hypergravity) on individual and evolutionary development of organisms, i.e., the role of gravity as a factor of evolution. At the present time, gravity biology has undergone considerable development.

Problems of the possible biological effects of heavy particles of primary cosmic radiation and other types of cosmic ionizing radiation served as a substantial impetus for the study and better understanding of distinctions of biological effects and relative biological effectiveness of corpuscular types of ionizing radiation. This was instrumental in development of new methods and means of radioprotection, investigation of effects of chronic exposure to radiation and different levels of the "natural" background of ionizing radiation, as well as augmenting our knowledge about the danger of nuclear weapons to mankind.

New, unusual and, in many cases, extremely unfavorable factors of space and spaceflights for living organisms served as an impetus for investigation of so-called extreme factors. Investigations pursued in recent years revealed that life is possible under extreme environmental conditions (extreme temperatures and barometric pressure, unusual gas composition of environment) that were previously believed to be incompatible with life. This enabled us to expand and deepen our conceptions of the range and limits of living conditions, mechanisms of biological adaptation and basic diversity of forms of life as the highest form of organization of matter.

Space medicine investigated the effect on organisms of flight factors and their combinations in greater depth, more systematically and over a considerably wider range of parameters than had been done before. For example, the effect of inertial-gravity forces was investigated comprehensively in the range from complete weightlessness to chronic and repeated hypergravity, from low accelerations to high levels that a crew could encounter, for example, during emergency ejection from a flight vehicle. Studies were made of the effects of accelerations in different directions, in relation to the axis of the body, including accelerations of changing directions and conditions. The results of this work made it possible to construct a rather orderly conception of gravity physiology, define permissible and optimum parameters and modes of gravity factors, develop means of protection against their adverse effects and of providing optimum conditions for life and efficient performance by crews.

The results obtained from these investigations are of interest to clinical biomechanics, traumatology and orthopedics, sports and forensic medicine.

Investigations of the effect on the body of such flight factors as vibration, noise, exposure to an environment with different gas composition and altered barometric pressure, at different temperatures, humidity, illumination, etc., were fruitful. All this, along with the developed protective measures and recommended standards constituted a contribution to development of industrial hygiene and occupational diseases, while the experience of working in pressure chambers turned out to be useful, for example, to clinical physicians in developing methods of hyperbaric oxygen therapy.

Formulation by space medicine of the problem of combined and associated effects of several factors, the results of which cannot be anticipated by investigating the different elements in the combinations, merits special attention. These facts, which were first discovered as far back as during the flight of Layka aboard the second artificial earth satellite, gained further development in the form of the conception of additive, potentiated or mutually neutralizing effect of a combination of different factors.

In general, all this is referable to the area of such a global and general human problem as "man and his environment."

There has been considerable development of problems of hypodynamia and hypokinesia, demonstrated by space medicine, which are attributable to weightlessness and limited active muscular activity and mobility of people during spaceflights. Numerous and diverse investigations in the laboratory, hospital and during spaceflights resulted in development of effective steps for protection against the adverse effect of hypodynamia and hypokinesia, and optimum regimens were recommended. Clinicians showed much interest in these problems and are actively continuing work on them.

As we know, space medicine discovered an unexpected and previously unknown phenomenon: change in fluid-electrolyte metabolism in cosmonauts. Numerous investigations (in clinostatic position, with head-down tilt, water immersion and weightlessness) "unraveled" to a considerable extent the extremely intricate interaction of reflex (in particular, from the ostium of the venae cavae), hormonal and other mechanisms that cause manifestation of this phenomenon, and made it possible to recommend a series of preventive measures. This problem also interested clinicians greatly, it is being studied by them extensively, while the results of investigations are used in flying practice.

The dynamics of the process of adaptation of the human body (in particular, the cardiovascular system) to long-term weightlessness and, what is even more difficult for the body, readaptation to earth's gravity after flights required prolonged, intense and in-depth investigation by specialists in space medicine in collaboration with the leading specialists in Soviet physiology, pathophysiology and clinical medicine. And, the question was posed considerably more broadly in order to solve this problem: What is adaptation? What is its range in different systems of the body? At what cost to the body is it achieved? To what extent is this adaptation final and stable? To what extent is it reversible after returning to earth's conditions? What are the chances of complete recovery? Of course, the problem acquires special urgency in this general medical and physiological formulation.

Space medicine devotes much attention to functions of the vestibular system, motion sickness, spatial orientation and spatial illusions experienced by many cosmonauts. It investigates vestibulosensory, vestibulomotor and vestibulovegetative reactions against the background of exposure to different combinations of flight factors as related to hemodynamic distinctions. Gaining deeper knowledge in this area is very relevant to clinical and aviation medicine.

Cosmonautics and space research provided a powerful impetus for intense development of biorhythmology, in particular, of daily or circadian, physiological cycles. The absence of natural alternation of day and night as pace makers of a 24-h cycle and the need to coordinate the work of cosmonauts with specific orbits, elements of orbits, sessions of communication with ground-based mission control centers made it necessary to conduct in-depth investigation of the possibility of altering circadian cycles of physiological and psychological activity, and to develop on this basis optimum sleep and wakefulness schedules. The studies conducted in this direction have found application in many sectors of the national economy that are related to shift work and guard duty, and in the broad sense in the global problem of "man and labor."

Much experience has been gained by space medicine in developing self-contained life-support systems in enclosed compartments. And, depending on the type and duration of missions, these systems can be based on different principles. As a result of many investigations, standards have been elaborated as to permissible and optimum parameters of gas composition, barometric pressure and other hygienic parameters of the environment. Group and individual equipment was developed that provides optimum conditions for living, efficient performance and flight safety, including cases of working in unique and emergency situations, extravehicular activity, scheduled and emergency abandonment of a spacecraft, ejection, landing on dry land or in the water with a parachute (G and altitude compensating suits and gear, airlocks and spacesuits with self-contained life-support system for extravehicular activity, and many others).

All this work on providing the artificial environment deepened our conceptions of the biosphere and contributed much toward solving problems of habitability of manned and working compartments; it made it possible to formulate the basic hygienic and sanitary requirements of the gas atmosphere and work place, define methods of protection against deleterious and toxic factors.

Progressive space engineering used many new (in particular, synthetic) materials, and this required prompt investigation of their potential toxic properties. Finally, space medicine investigated regularly problems of nutrition and water supply for crews, metabolism during flights and under various extreme conditions. The need for cosmonauts to spend a long time in a closed and confining area led to investigation of questions of space immunology and microbiology, which yielded some rather valuable information. The results of this work are of equal interest to public health, sanitation and hygiene.

Specialists in space medicine participated actively in developing a system to search for crews after dry or wet landings, rescue them, render first aid and evacuate them. Much has been done to refine the method of cosmonaut training, in particular, in the area of self-contained survival of crews that suffered an accident and found themselves under extreme conditions for survival and adverse climate and geographic conditions. This work is unquestionably important to such branches of medicine as medical geography, distinctions of state and reactions of healthy and sick people in regions with different climates and geographic zones, as well as for the branch of science that is called "survival medicine."

In 25 years, space medicine has undergone considerable evolution. While at the early stages of its development attention was focused mainly on the study of autonomic and somatic functions, the center of gravity of research was subsequently shifted to animal and psychological processes involved in professional work capacity and efficient performance by crew members. In developing space technology, psychophysiological capacities of man and his physiological and hygienic requirements were scrupulously taken into consideration. Along with design engineers, medical specialists, psychologists and the cosmonauts themselves participated in developing spacecraft, life-support systems, controls and indication systems (information displays).

This progressive ergonomic principle of medical and psychological involvement in new equipment had a beneficial influence on development of space medicine and placed it among the leaders in progress of ergonomics and engineering psychology. The so-called principle of engineering psychological design, which is a mandatory law of cosmonautics and space medicine, has improved substantially the adequacy of cabins, work place and environment, as well as systems of display and control, to psychophysiological characteristics and capacities of crew members, and the professional tasks put to them.

Systematic consideration of human characteristics makes it possible to bring to life the conception of designing the work of cosmonauts under different flight conditions and modes, i.e., to elaborate optimum algorithms of human performance, provide optimum distribution of duties between man and machine, which should assure efficient and safe operation of space equipment.

In this direction too, as we see, space medicine was able to make its contribution to the study of global problems of our times, "Man and machine," "interaction of man and work tools during performance of work."

Intense investigation of the work of spacecraft crews under extreme conditions led to deeper knowledge about psychoemotional stress, strain and fatigue caused by professional activity, guidelines for setting standards of flight load, work and rest schedules.

Investigations conducted in anechoic pressure chambers on individual subjects and small groups of people disclosed many psychological distinctions related to prolonged exposure of operators to social and physiological isolation, their performance under these conditions, shortage of information, stimuli and motor activity, and they made it possible to study professional interaction and psychological compatibility of crew members. These studies were instrumental in preparation of recommendations on improvement of psychological support of flight crews, optimum manning of crews with due consideration of psychological distinctions of members, optimization of distribution of duties among them.

Specialists in space medicine turned out to be trail blazers in matters of medical and psychological screening of cosmonauts. Although they were guided by the positive experience in screening pilot candidates, they had to solve many difficult problems, as well as some specific to cosmonautics (in particular, those related to prolonged work by cosmonauts under conditions of sensory and social deprivation, adynamia, psychological compatibility of crew members, etc.).

And they had to start from scratch in constructing a program for cosmonaut training for forthcoming missions. It must be stated that specialists in space medicine coped well with this task. They wisely combined theoretical and practical, nonspecific health-improving and specific professional, physical and moral-volitional, simulator and flight forms of training. In these 25 years, the program of medical and psychological training was significantly improved and had a beneficial influence on development of programs of training for the most varied types of special professional work.

The system developed for dynamic medical observation, expert determination of fitness for flights, meticulous medical monitoring during preflight training and spaceflights, in-depth examination and observation after flights also merits attention. To solve problems of expert evaluation of fitness, work capacity, setting work load standards, work and rest schedules, rehabilitation after flights and various diseases, it was necessary to investigate such basic general medical and physiological problems as determination of the range and criteria of the norm and pathology, functional disorders and premorbid states, range of fluctuation of normal physiological parameters in different individuals and groups, at rest and with a load, during development of fatigue and overtiredness. The work to determine the "individual norm" for specific conditions was particularly important and difficult. The ranges of standards set by the World Health Organization are too wide. Sophisticated modern methods are needed to establish "physiological and biochemical individuality." Space medicine has made some contribution to this problem as well, as it constantly refines existing methods, develops new ones and determines their informativeness.

As we have already mentioned, space medicine was able to involve specialists in many directions in their work: engineers, biologists, clinicians, psychologists, etc. This advanced the methodological armamentarium to a new and higher level. Space medicine, along with specialists in allied fields, developed miniaturized electronic equipment for automatic and remote recording of basic physiological, psychological and hygienic parameters, biotelemetric transmission of data, automatic processing and storage of the latter, as well as for diagnostication. As a result, we are now able to implement inflight medical monitoring of physiological and mental condition of crews, the quality of their professional performance.

New methodological and technical possibilities opened the way for modeling and investigation on models of algorithms of different types of work, physiological and psychological states. Computer hardware is used extensively. Various high-speed methods have been developed for clinical tests, in particular biochemical ones.

The new methods of investigation and refined equipment produced in the interests of space medicine have gained wide application in public health, industrial and sports physiology. For example, a portable multichannel apparatus was developed on the basis of modern radio electronics, which permits simultaneous recording of several physiological parameters in a comparable form for integral evaluation of the condition of an individual and of his different organs and systems. Along with special attachments, this apparatus can automatically record the status of working subjects who are far away for a long time without

causing them any significant discomfort. Special programs (algorithms) on magnetic tape permit immediate interpretation of a large amount of medical data using a computer.

The method space medicine developed for applying negative pressure to the lower half of the body (using a vacuum bladder) gained further development as a rather sensitive method of delivering a graded functional load to the cardiovascular system.

There has been refinement of methods of volumetric oscillography, which permit examination of vascular lumen even in the presence of interference, as well as plethysmography, ballistocardiography, seismocardiography, etc. Diagnostic ultrasound Doppler cardiography, which locates muscular structures and valves of the heart, permits determination of the functional state and individual distinctions of coronary circulation, as well as evaluation of changes in cardiac output, has gained wide use.

We should also mention the active adoption of various specific and nonspecific load tests (for example, the hypoxic test), in order to demonstrate the body's reserves or latent pathology (for example, prenosological changes in coronary circulation).

We can also mention advances in the field of space pharmacology (phenibut and other agents) and space microbiology (methods for examining intestinal flora, demonstrating and cultivating asporogenic anaerobic bacteria and lactobacilli, etc.), with regard to development of equipment such as the magneto cardiograph, "artificial ear" instrument for metrological checking of audiometers, electrostimulator of muscles and general purpose training device for the skeletomuscular and articular system of bedridden patients, miniaturized Telekont (300 g) biotelemetry apparatus and catheters with antithrombogenic properties, and many others.

It is important to note that such a progressive and rapidly developing science as cosmonautics, that is on the boundary of many disciplines, put to space medicine new and unexpected questions that required unusual approaches, nonstandard thinking, involvement of representatives of other specialties in order to furnish immediate answers, and this could not help but have a beneficial effect on advancement of qualifications of personnel. The problems solved by space medicine constituted a remarkable dialectical unity of practical applied significance and high theoretical interest with respect to progress of basic sciences.

The combination of theory and practice provides space medicine with exceptionally favorable methodological opportunities to check the validity of its theoretical developments. For example, the successful design of an artificial environment in the spacecraft cabin is the best practical criterion of our true knowledge about the biosphere, relations between man and his environment.

Cosmonautics and its constituent--space biology and medicine--play a large and fruitful scientific-social and political role. They are instrumental in mutual understanding of nations, collaboration, progress and peace in the entire world.

Successful exploration and exploitation of space constitute a global task, which only the combined efforts of all states and nations can perform. Such organizations as the International Astronautical Federation, International Academy of Astronautics, the interacademic organization COSPAR and others play a positive role in the area of exchange of scientific information on these matters. Collaboration of different countries in space investigations favors progress and integration, standardization and unification of their scientific and technological potential.

The Intercosmos organization of socialist countries is a good example of such collaboration; its program is followed in the performance of a large number of scientifically rather valuable joint investigations aboard unmanned Soviet spaceflight vehicles and Salyut-Soyuz orbital complexes, aboard which cosmonauts from nine socialist countries worked as part of rendez-vous crews, as well as cosmonauts from India and France. At the present time, preparations are under way for a Soviet-Syrian crew mission.

Everyone remembers the successful Soviet-American spaceflight on the Soyuz-Apollo program. In 1975, Soviet and American specialists published a comprehensive joint work, "Bases of Space Biology and Medicine" (simultaneously in Russian and English). Our journal, KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA is translated into English in the United States. American authors publish their works in our periodical from time to time, while Soviet specialists do so in the analogous American periodical.

All this gives us grounds to hope that common sense will prevail, and that space will become the area for peace, collaboration and progress.

In conclusion, it should be noted that, in 25 years, space biology and medicine has traveled a long and meaningful road. However, it will have to solve even more complicated problems in the future. Specialists in space biology and aerospace medicine will spare no effort to make their contribution to this great cause, at the start of which Yuriy Alekseyevich Gagarin participated.

UDC: 613.693-07

STAGES OF DEVELOPMENT OF THE PROBLEM OF FLIGHT SAFETY IN AVIATION MEDICINE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 5 May 85) pp 12-19

[Article by V. A. Ponomarenko]

[Text] Aviation medicine as a branch of medical science is a direct participant in technological progress in aviation. The high level of development of aviation equipment at the present stage would be inconceivable without adequate solution of problems of its control by man.

In past years, aviation medicine was enriched with new theoretical conceptions and vast practical experience in the area of assuring flight safety. New "growth points" emerged, both in aviation medicine proper and at its boundaries with allied disciplines in engineering psychology and ergonomics.

Organization of protection of man on the basis of providing an optimum environment was recognized as the key direction of scientific research at the first stage of development of aviation medicine, since in essence it determined assurance of human vital functions and work capacity.

Practical implementation of the basic ideas of protection of an individual connected into a technological system was based not only on advances in applied physiology, but new investigative methods that permitted gaining deeper understanding of the biological bases of adaptation to a unique environment and disclosure of mechanisms and patterns that control processes of interaction between the environment and man.

It should be noted that it is expressly in aviation medicine, in determining the physiological bases of reliability of the human body, that modeling was developed as a fundamental means of learning the laws of interaction between man and an aggressive environment. Adverse flight factors were simulated: hypoxia, impact overloads, angular and linear accelerations, vibration, heat, etc. Accordingly, equipment was developed (pressure chamber, centrifuge, vestibular, ejection stands, etc.) that permitted simulation of environmental conditions. Specialists in aviation medicine used models to determine the physiological ranges and levels of compensatory capacities of the body during exposure to extreme factors; they established the sequence and structure of processes of physiological adaptation; they validated means of protecting the pilot that would assure his ability to function and efficiency.

For the first time in the history of medical science, in accordance with the teaching of I. M. Sechenov and I. P. Pavlov, aviation medicine disclosed the laws of adaptation and conditioned reflex activity in an unusual environment. In particular they worked out the mechanisms of control of hemodynamics, digestion and metabolism under conditions of altered gravity, mechanisms of impaired function of analyzer, respiratory, cardiovascular and hemopoietic system during exposure to radial accelerations, hypoxia, noise, vibration and other flight factors, mechanisms of spatial orientation in the presence of distorted visual and vestibular afferentation, mechanisms of adaptation to extreme effects of the gas atmosphere and impact loads.

Practical use of the results of scientific research in aviation medicine was implemented by the work of aviation physicians, not only along the lines of medical monitoring and expertise, organization of living conditions, nutrition, recreation and training of flight personnel, but in the area of introduction of validated recommendations and suggestions pertaining to aviation equipment. We can single out two levels of solving this problem, viewing assurance of flight safety as the basic direction of aviation medicine.

The first level is materially functional, on which medical research is aimed at assuring man's safety in the cockpit of a flight vehicle.

On this level, thanks to the efforts of scientists and practical workers, it was possible to develop biological, physiological and hygienic protection, which virtually eliminated mortality and reduced to a minimum disability due to the direct effect of adverse flight factors, reduced appreciably occupational traumatism, stabilized occupational morbidity with increase in complexity and difficulty of flight work, and made it possible to develop a system of functional simulators in order to extent professional longevity.

Thus, the above achievements on the first level of providing flight safety were instrumental in creating a new category in solving this problem, namely, prevention of flight accidents. However, further improvement of aviation equipment and expansion of the tasks and means of using it required methodological and ideological re-equipment of aviation medicine in order to reassess the new qualitative phenomena in the structure of flight work and improve reliability and efficiency of aviation specialists. These qualitative changes consisted mainly of some stabilization of the extent of adverse effects of physical environmental factors on man against the background of drastic increase in mental and emotional tension.

This circumstance required thorough investigation, from the standpoint of the human factor, of the qualitative transformations that were observed in new and particularly promising aviation equipment. Among the most significant changes having a basically important effect on the performance of flight personnel, we should mention the following: automation of data processing and, consequently, change in structure of such a mental act as decision making; automation of controls for rudder surfaces of flight vehicles, which created a contradictory situation--monotony against the background of heightened readiness for action; introduction of radio electronic equipment which altered appreciably the principles, types and forms of coding signals about the status of aircraft systems and units; appearance of new physical factors,

which require new organization and construction of protective gear; increased dynamics with respect to alternation of type and form of received signals in the course of a single flight, which require not only automated skills, but formation of functional lability of mental processes.

From the medical point of view, all these changes can be viewed as potential risk factors to psychosomatic health. Experience shows that not only somatic health, but psychophysiological limitations of man hold back the realization of capabilities for technological progress. In other words, as the problem of preserving health was being solved, the problem of results obtained by aviation specialists arose. Of course, one should not deny the dominant role of the health factor in aviation medicine, which has always stood out as the limiting indicator of humanistic content of technological progress. However, at the present time, aviation medicine must apply more purposeful efforts in order to enhance the efficiency and reliability of the man-flight vehicle-environment system and form the second level of assuring flight safety, the systemic-goal-oriented level, on which medical investigations are directed toward assuring man's safety during performance of a flight assignment. The methodological basis of medical research on this level is systems analysis. This means that elements of the work environment (special gear, rescue equipment, view from the cockput, microclimate, clothing, controls, instruments, signaling devices), which emerge as factors that have an effect, are not considered by themselves, or by their specific influence, but from the standpoint of systemic aggregate quality (to what extent each element helps or prevents achievement of the general goal that is before the pilot). On this basis, the conditions under which crew members work or, as it is generally expressed, the environment acquires a new content, the substance of which lies in the fact that both the physiological-hygienic conditions in the cockpit of the flight vehicle and vital functions of the body, and finally work capacity are contained in the same pilot-aircraft-environment system. This attitude toward working conditions offers distinct orientation to the effect that reliability of the pilot-aircraft-environment system is defined as the probability of achieving a specified result without detriment to human health or life and with preservation of the aircraft.

Of course, such a point of view requires a change in way of thinking and practical activity of aviation physicians, with due consideration of the new meaning imparted to the concept of "environment" [or habitat], which implies an environment that provides for reliable performance. With this approach, one should apparently use environment to refer to the set of physical and psychological factors that affect the pilot during his interaction with equipment and which alter reliability and efficiency of the pilot-aircraft-environment system.

Apparently, it is expressly delayed redirection of scientific thinking toward systems analysis of human performance when controlling a flight vehicle that led to the fact that technological progress in aviation "legitimized" the machinocentric approach (from machine to man). As a result, a stable stereotype of thinking was formed, which acknowledged the following theses: efficiency and reliability of man in a control system are achieved primarily through practice and training, i.e., mathcing the pilot with the equipment that is being developed; the machine can perform any operation, while the efficiency and safety of its operation depend on organization and control.

Evidently, the technological revolution is also called upon to alter some stereotypes in engineering policy, in particular, to make fuller use of the results of medical and psychological investigations of performance when designing work places and information displays to assure good performance.

The distinctions of the second level of assuring flight safety in aviation medicine can be illustrated on the example of using conceptions of personal and human factors. Here it should be noted that, although the second level is most probably attributable to the influence of new directions in aviation medicine (psychophysiology, engineering psychology), it provides first of all for safeguarding health, provided that the "health" category is combined with the "performance" category, and that both are contained in the integral parameter, "reliability of human factor." We refer to human health as a component characterizing the result of work. Such formulation of the matter requires new orientation, not only with respect to preserving health as such, but involvement in formation of the integral trait of pilots, professional reliability. Professional reliability of a pilot implies that there is a link between health status and reserve capacities of the body. As a rule, a decrease in professional reliability is defined by the concept of "personal factor," i.e., when deviations of health status or lack of required abilities were related to the cause of an accident.

It is known that the concept of "personal factor" was introduced into medical practice as a criterion determining fitness of an individual (primarily his health status) for professional work--flying. At first, this concept was used only in medicine, since it was dealing with professional fitness. A man could be essentially healthy, but not have the health needed to master flying as a profession. Then "personal factor" acquired the status of an explanatory guideline in the cause of another phenomenon--accidents, i.e., mistakes that resulted in breakdown, emergencies and even disasters. At this stage, aviation medicine began to use the content of the concept of "personal factor" as a methodological direction in the search and determination of the nosological forms, individual psychological personality trates and functional states that presented a threat to safe flying.

Thus, great advances were made in aviation medicine in that period. By that time, there had been investigations of flight factors, occupational hazards and occupational nosology; a system of preventive measures was elaborated, including expert evaluation that did not permit occupational diseases and accidents that were directly related to health status.

The "health" category acquired special meaning in the social system of responsibility for flight safety. From this emerged a strict, orderly medical system, validated by experience, for screening, dynamic observation, expert certification and the scientific directions that implemented this system.

However, the aviation physician, in providing for retention and maintenance of professional reliability of pilots, must relate the concept of personal factor to professional health. Herein is the substance of the first thesis mentioned above. It is necessary to define specifically the concept of "professional health" and the scientific and practical corollaries that ensue from it.

Thus, professional health is the body's property to retain specified compensatory and defense mechanisms that provide for work capacity under all conditions of professional activity.

The restoration of functional state in accordance with the stipulated volume and type of professional work is a systemic trait of a pilot's professional health status.

Let us discuss the beneficial changes in organization of medical support of flights that we can expect if the conception of professional health is assimilated.

In aviation practice. This conception calls for a shift from an empirical position to a scientific one, and it permits basic change in the procedure for allowing pilots to fly in accordance with medical indications, enriching and enlarging it with the process of forecasting the functional state and its conformity to the piloting tasks. Such an approach will make it necessary to learn methods and procedures for testing, activation and correction of functional state, development of methods to monitor restoration of an altered working state. In other words, medical monitoring is acquiring a new direction, where not only the diagnosis, but functional state is related by the physician to the difficulty of performing a specific professional task. Maintaining this state becomes and important function for the aviation physician, and if this is achieved in practice, there will be activation of scientific development of recovery [rehabilitation] theory. Recovery does not refer solely to optimum types of therapy and rest. It is the formation of new functional systems and connections with a high level of compensation and even substitution of some functions by others with exposure to extreme factors. There is flight training and there is sociopsychological training, but there should also be medical training of professional health. Herein expressly lies the great meaning of the positive social interaction between physician and pilot.

At the present time, the personal factor is sometimes associated with deficiency. For this reason, expert medical certification of pilots is oriented toward developing functional tests that would be pathognomonic for professional performance. For example, the well-known bicycle ergometer test definitely reveals latent ischemic heart disease, but unfortunately it deprives some pilots of their occupation, in spite of the fact that their professional health status conforms to the conditions under which they work. It is expressly this orientation that must refine developments in the area of psychosomatic, psychopharmacological, sociopsychological and professional-training agents aimed at restoring professional health.

In aviation medicine. The conception we are discussing enables us to pursue new scientific searches. First of all, there must be further development of physiological theory of adaptation with consideration of immunological and evolutionary mechanisms of controlling interaction between the body and an aggressive environment. It is only through such basic research that one can elaborate validated guidelines for setting hygienic standards that take dialectically into consideration the conception of allowable risk on the basis of priority of medical and biological indicators over economic ones. And, finally, the conception of professional health will serve as an impetus for

development in aviation medicine of new methods and equipment, including devices that are exploratory, test the reserves of the cardiovascular, respiratory and hemopoietic system, and many aspects of metabolic processes.

In organization of medical support of flights. The conception of personal factor as we have interpreted it calls for preparation of an integral program for the problem of control and protection of professional health. Such a program should begin with classification of occupational hazards and definition of their link with epidemiology of occupational diseases or diseases caused by flight factors and living conditions of groups of flight personnel. This will result in medical suggestions we developed for industry and management with respect to social steps for raising and preserving the level of health in accordance with development of aviation equipment and increasing difficulty of tasks. The results of fulfilling the program for assuring occupational health will serve in the future as the basis for medicotechnical specifications pertaining to equipment and working conditions: human reserves are not to be exploited, but developed by means of purposeful activation of sense organs, intelligence, emotions, memory and satisfying social needs.

We think that such a program could animate and deepen scientific research in the area of establishing links between partial health deficiency and occupational reliability. The modern individual approach does not solve this problem entirely, and for this reason preventive measures are sometimes replaced with grounding.

It should be recalled that medicine always based itself on profound knowledge of the bases of life itself in its treatment of diseases. The same can be said of aviation medicine, which would be inconceivable without delving into the lifestyle of pilots.

It is apparent to every aviation physician that to ground a pilot means to deprive him, first of all, of his main occupation, and for some pilots, to also deprive him of the meaning and value of life.

In this regard, we consider it opportune to advance the second thesis: mandatory sociologization of the medical component of the concept of personal factor.

Like no other science, aviation medicine observes, studies and tests man at the limit of his capacities and actions under extreme conditions, when both greatness of spirit and strength of body are manifested, as well as dynamics of functional disturbances in integral systems. Expressly the thesis of sociologization really puts a task to us: to reform and alter properties of the body and personality pertaining to physical, mental, ethical and moral aspects that are instrumental in flight work longevity, motivated orientation toward achievement of high results, i.e., development of capacities for homeostatic reactions to the different complexities of flight work. It is assumed that the problem of the personal factor will acquire expressly such meaning in the near future.

But for the time being, since the personal factor is sometimes equated only with unreliability of the man-machine system, it became necessary to elaborate

a conception about the human factor. Separation of causes and effects in such a complex phenomenon as interaction of man and machine constitutes its medical meaning.

The concept of "human factor" was formulated on the basis of the teaching of A. G. Shishov about interaction of man and machine and causation of some mistakes by flaws in the information environment; this concept combines all of the variables that affect reliability and efficiency of interaction between man and machine. In other words, the concept of human factor contains psychological characteristics, capacities and limitations of analyzers, the psyche, consciousness, conditioned reflex activity under the concrete conditions of performing an erroneous action that are inherent in all people, rather than a given individual.

We believe that in investigating the causes of flight accidents, it is more expedient to be governed by the concept of human factor which systemically combines all aspects of aviation life. And it should be noted that the conception of human factor adds a new aspect of flight that is not always convenient to the system of medical support. The fact of the matter is that its assimilation implies some reorientation of the medical service in the matter of assuring flight safety. First of all, assuring flight safety from the standpoint of the human factor refers not only to assuring health and vital functions of a pilot, protecting him against adverse flight factors, but also to providing conditions, starting with screening, regulation of flight load and ending with medical and technical specifications for the work place that would be instrumental in improving professional efficiency. The conception of human factor reflects the systemic approach, and for this reason medical support of flight safety also covers questions of reliability of the entire pilot-aircraft-environment system, both during operation of aircraft and its equipment, and at the stages of their development.

Thus, through its development aviation medicine has come to a point where it experienced an objective need for establishing a new experimental base that would enable our science to anticipate technological progress in some way, rather than follow it. In other words, we are again dealing with prevention of accidents and forestalling decisions to coordinate human capacities with aviation equipment. In accordance with this methodology, preservation of mental and physical health is determined by the principle of prompt checking of equipment and conditions of future work of pilots. The armamentarium of aviation medicine is being enlarged with special modeling complexes that permit exploratory investigations. Models of new working conditions help develop new methods of clinical and physiological evaluation of work capacity and means of psychophysiological rehabilitation. But the main thing is that it is possible, with use of modeling (design) of future performance, to produce conditions that would prevent human error in the control system. There is a class of errors where the crew is merely the carrier of a threat to flight safety, whereas circumstances that are not always by far dependent on them are the immediate source [of error]. We are not dealing here with either inconvenience or anthropometric discomfort, but with the fact that psychophysiological laws of psychomotor activity in interaction with machines are not always taken into consideration. Among them, we can mention the dominant state, orienting exploratory reflex, sense of time, goal reflex,

differentiated inhibition, visual and vestibular illusions, postural reflexes and others. All of the foregoing is the basic evolutionary characteristic of man. And if the task that the crew is to perform is in contradiction with these laws, conditions appear for unreliable action. If, for example, while piloting an aircraft angular accelerations of more than $12°/s^2$ appear, postural reflexes will elicit body and limb movements, regardless of the individuals will and awareness, in the direction opposite to the accelerations. During flight, this could be expressed by a movement of the control to one side, whereas instructions call for a movement down to reduce the angle of attack, or by an involuntary foot movement, which would lead to slipping of the aircraft and, consequently, a piloting error.

Thus, the conception of human factor enables us to conclude that the error category is contained in the system of human performance. Consequently, error emerges as an integral property characterizing interaction of the man-machine system, and it is the first, rather than last, element in the cause and effect relations of development of a flight incident. The conception of human factor directs aviation medicine toward establishing relationships between physiological and hygienic working conditions, on the one hand, and the crew's work capacity, on the other. It is felt that the system of introduction of medical recommendations would be more efficient and effective if part of the errors would be referred to the area of the human factor. This means that, in the presence of professional training, professional health and discipline, an individual would make an error due to failure to fulfill some sanitary, hygienic or psychophysiological requirements of professional working conditions and equipment.

Such formulation of the matter requires that existing systems of objective monitoring be supplemented with equipment that records the level and duration of exposure to noise, vibration, temperature, gas composition of cockpit atmosphere, etc. Only in this case would it be possible to differentiate between causes of errors that occur due to inadequate professional training or due to exceeding human capabilities. The conception of human factor in aviation medicine provides, to some extent, a new orientation toward utilizing the achievements of technological progress in the interests of man's safety. We refer to the fact that one should also provide a "human modulus" in modern onboard computer complexes, which would constitute a bioengineering system of control of the environment in the cabin of a flight vehicle with automatic reflection in protective equipment and, in its absence, display on signaling instruments.

Aviation physicians are developing the most actively the principle of biological feedback for control of condition of the body. At the same time, use onboard flight vehicles of rapid-action onboard computers that have a large memory should also direct them toward monitoring the physical state of the environment. Physiologists are expected to elaborate baseline data, which would define with a probablity of, let us say, at least 0.95 the zone of high, diminished and low work capacity. In such a case, when maximum permissible levels are reached (for example, of vibration, noise, temperature, electromagnetic radiation, gas composition, barometric pressure gradient), the appropriate protective system should turn on automatically. It is believed that at this stage, instrument monitoring of the environment is more realistic than the same monitoring by means of the body's biological sensors.

Thus, aviation medicine as a science and the practice of medical support of flight safety, as well as expertise, requires expansion and some revision of tactical approaches, with retention of the cardinal strategy aimed at safeguarding health. Man as a biosocial being changes, particularly the motives for his behavior and actions. Not infrequently, these are morbid [painful] changes. For this reason, aviation physicians must concentrate their attention to proventive work and preclude a pilot's inadequate or morbid reaction. Evidently, herein lies the essence of the humanistic direction of aviation medicine in the matter of assuring flight safety.

SURVEYS

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INTERLABYRINTHINE ASYMMETRY, VESTIBULAR DYSFUNCTION AND SPACE MOTION SICKNESS

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[Article by G. I. Gorgiladze, G. I. Samarin and I. I. Bryanov]

[English abstract from source] The data available suggest that a disorder in the labyrinthine paired function can be regarded as a factor responsible for the initiation and development of space motion sickness. This concept is based on the assumption that in the norm the vestibular function is to a certain extent asymmetric which is made for by a compensatory center in the central nervous system. Exposure to an unusual space environment leads to a disorder of this compensation and development of a "new" vestibular asymmetry. This exposure involves: elimination of the difference in the weight of otolith membranes, disorder of the canal-otolith interaction, asymmetric blood-CSF changes, distinct interhemispheric asymmetry, general stress. Vestibular asymmetry that develops in the weightless state may become sufficient for the generalization of afferent impulsation to normal stimuli and development of a strong reaction. Adaptation to weightlessness occurs due to rearrangements of the compensatory center which are responsible for lower vestibular asymmetry. The compensatory mechanisms that have evolved in weightlessness continue to function during a certain time interval after recovery. They facilitate a re-initiation of vestibular asymmetry and motion sickness that is mainly provoked by head movements, as in the weightless state.

[Text] Transient functional disturbances occur in some systems of the body, mainly those whose function is related to earth's gravity field, during spaceflgihts under the influence of the unique physical environmental conditions: cardiovascular, skeletomuscular and vestibular. Vestibular disorders are manifested in the form of illusions, spatial disorientation, vertigo and, occasionally, in the form of nausea and emesis--the so-called space motion sickness (SMS). The return to earth is often associated with recurrence of these phenomena [7, 12, 61, 74].

Analysis of data obtained from clinical and physiological examination of cosmonauts leads us to consider disturbances referable to paired function of

the labyrinths as one of the causes of onset and development of SMS. Thus, the presence of more or less noticeable initial vestibular, in particular otolith, asymmetry was noted in cosmonauts who reported varying degrees of SMS symptoms during flights. After returning to earth, in the acute recovery period, many cosmonauts presented reliable asymmetry of different parameters of vestibular function. Marked otolith asymmetry, as demonstrable by the counterrotation reaction of the eyeball, reached 18-19°. Canal asymmetry increased 3-4-fold. There was asymmetry of oculomotor reactions to oppositely directed optokinetic stimuli. In addition, there was increased asymmetry of perception of spatial coordinates with the body in lateral position (to 14°, versus baseline asymmetry of no more than 5°). As a rule, vestibular asymmetry was associated with symptoms of motion sickness. Marked motion sickness was observed expressly in those cases where vestibular asymmetry was at a maximum, being manifested in the form of spontaneous or positional nystagmus [24, 26, 37, 61] (Figure 1).

A state in which there is complete elimination of function of one of the labyrinths is the most graphic manifestation of the link between interlabyrinthine asymmetry and vestibular dysfunction. This is associated with disturbances in basic elements of the vestibular system: fixed gaze, retention of equilibrium and spatial orientation. In animals, unilateral labyrinthectomy elicits deviation of the eyes and nystagmus, turns and tilts of the head and rolling to the side of the missing labyrinth, assymetrical position of limbs, faster heart and respiration rates, blood pressure drop, activation of EEG, etc. [21, 100]. In man, destruction of the labyrinth as a result of surgical intervention is associated with nystagmus, disorders referable to static and dynamic equilibrium, gaze fixations in the form of development of Dandy's symptom, vertigo, nausea, vomiting [51, 53, 89, 91, 119, 120). In time, these signs diminish and partially disappear due to central compensation manifested by gradual restoration of bioelectrical activity of neurons of vestibular nuclei and the deafferented side [22, 105, 109]. However, this compensation is usually not complete, and for this reason only leads to attenuation of internuclear vestibular imbalance, rather than its elimination. This is indicated by the consistently demonstrable asymmetry of evoked reactions to oppositely directed stimuli that are the same in magnitude to receptors of the intact labyrinth and preservation in unchanged form of some manifestations of vestibular dysfunction [21, 83, 100, 115]. The compensation is rather unstable. It is impaired when there is change in spatial position of the head, under stress, with exposure to ionizing radiation, anesthesia, various pharmacological agents, alcohol, hypothermia, hypoxia and in a water environment [9, 13, 21, 38, 51, 56, 80, 104, 115]. Special mention should be made of the fact that impairment of vestibular compensation, in the form of recurrence and intensification of attenuated consequences of unliateral labyrinthectomy, was observed in weightlessness during parabolic flight [33, 92].

The obtained data warrant the assumption that, on the one hand, there is a constant component of compensation that arises and develops as a result of intracerebral plastic changes and, on the other hand, a dynamic component. The latter arises because of inhibitory influence of visual and proprioceptive signals on vestibular centers. Thus, in subjects with unilateral elimination of vestibular function, during visual fixation there is rather rapid disappearance of nystagmus and deviation of the body to the involved side when walking,

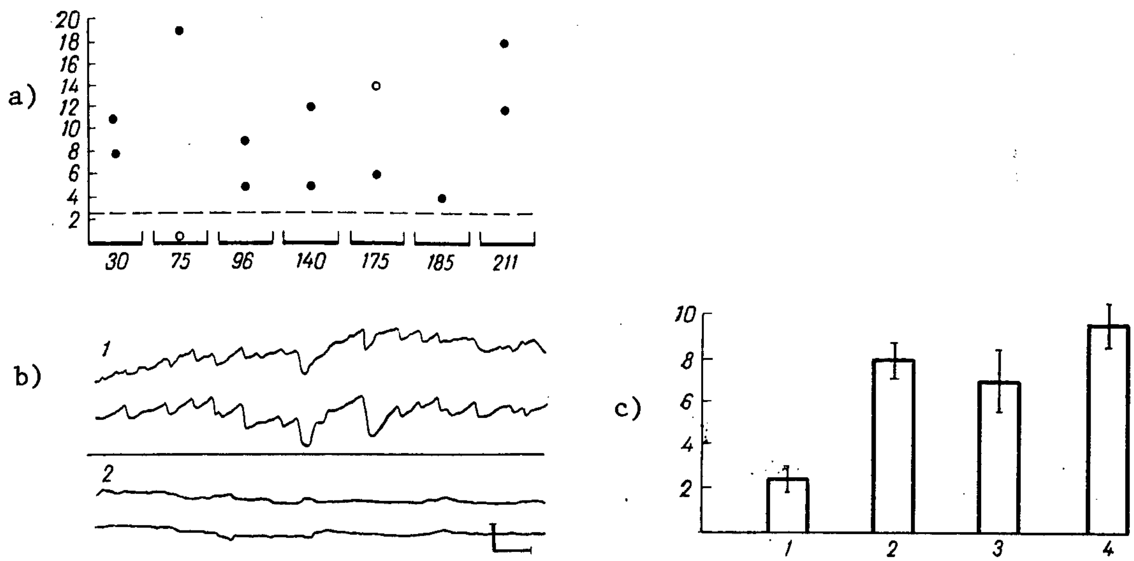

Figure 1. Manifestations of vestibular asymmetry in cosmonauts and healthy individuals during simulation of some spaceflight factors

a) otolith asymmetry in cosmonauts immediately after orbital flights; ●--cases of development of marked motion sickness, o--no motion sickness; x-axis--orbital flight days, y-axis--magnitude of asymmetry of eyeball counter-rotation reaction (degrees); dash line--mean level of this reaction in healthy males [37, 61]

b) spontaneous nystagmus in crew member of Soyuz-T-4--Salyut-6 orbital complex after 1 h (1) and its absence on 56th day (2) after completion of 75-day orbital flight; top and bottom curves--electrooculogram in vertical and horizontal leads, respectively; calibration: 10°, 1 s

c) otolith asymmetry of eyeball counterrotation reaction (degrees) in healthy subjects under normal conditions (1), after 182-day hypokinesia with head-down tilt (2), after experimentally induced motion sickness in response to Coriolis and precession accelerations (3) and in cosmonauts immediately after long-term orbital flights (4); here and in other figures, vertical lines indicate one standard error [37]

whereas in the dark the manifestations of vestibular asymmetry were consistently observed [51]. In animals submitted to unilateral labyrinthectomy, elimination of vision or static load led to immediate appearance of asymmetrical postural reactions and nystagmus [14, 22, 100]. It is also opportune to recall that spontaneous (or physiological vestibular) and positional nystagmus has been demonstrated in many healthy people (89% of the cases, according to some reports), with prevalence on one side or the other, which was not present during visual fixation [28, 29, 66, 73, 76]. It was recently found that spontaneous nystagmus can be removed by passing direct current of a specific direction through one labyrinth [29]. This phenomenon should apparently be attributed to the fact that there is complete "balancing" of afferentation from both labyrinths. Such an interpretation is confirmed by the results of

investigations, in which interlabyrinthine asymmetry induced by exclusion of one labyrinth was compensated by passing through it direct current in an ascending direction, and this eliminated the consequences of unilateral labyrinthectomy [23].

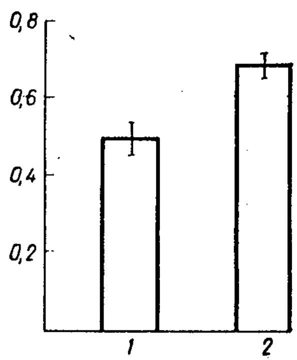

Figure 2.
Weight difference between utricular (1) and saccular (2) statoliths in right and left labyrinths of 25 adult specimens of Esox lucius (pike, in mg); $P<0.05$ in both cases

Onset of vestibular dysfunction with sensory and autonomic manifestations in weightlessness and upon return to earth can be described as follows. Dynamic equilibrium, which is present between vestibular nuclei on both sides because of so-called labyrinthine tonus, is apparently never complete. This happens because the vestibular nuclei of one side are constantly exposed to greater excitatory or inhibitory influence of labyrinthine receptors, other sensory inputs, as well as different elements of the central nervous system. Asymmetry of weight [30, 54], volume [45], otolith membranes (Figure 2), as well as anatomical and spatial asymmetry of semicircular canals, proprioceptive and interhemispheric asymmetry, are some of the causes that could be mentioned for appearance of internuclear vestibular imbalance. Thus, the latter would consist of asymmetry of labyrinthine receptors and asymmetry due to access of asymmetrical extralabyrinthine signals into vestibular nuclei. Apparently, internuclear vestibular imbalance also increases as a result of intensification of inhibitory effect of vestibular nuclei that are in a more active state upon the corresponding nuclei of the contralateral side due to presence between them of reciprocally organized commissural connections, as well as activation of nerve elements that are the origin of centrifugal nerve fibers of the vestibular nerve and have an inhibitory effect on afferent activity of receptors of the contralateral labyrinth [15-19, 95, 101, 103, 114, 118]. This state can be referred to as a latent form of vestibular asymmetry (Figure 3,I). The imbalance that then arises between vestibular nuclei on both sides is compensated by the compensating (balancing) center formed in the central nervous system. Vestibular nuclear imbalance is leveled off in view of intensification of inhibitory influences on the side of prevalent activity and of alleviating influences on the side with less activity. Both vestibular nuclei and labyrinthine receptors on the side of prevalence are subject to inhibition due to increased impulsation activity of the afferent inhibitory pathway (Figure 3,II).

Thus, the functional vestibular asymmetry that is present under ordinary conditions on the ground is leveld off as a result of central compensation. Spaceflight extreme factors lead to impairment of this compensation and cause appearance of a "new" vestibular asymmetry. The conditions for this may be disappearance of difference in otolith membrane weight, impairment of canal and otolith interaction, asymmetric changes in blood and spinal fluid dynamics, development of marked interhemispheric asymmetry and stress.

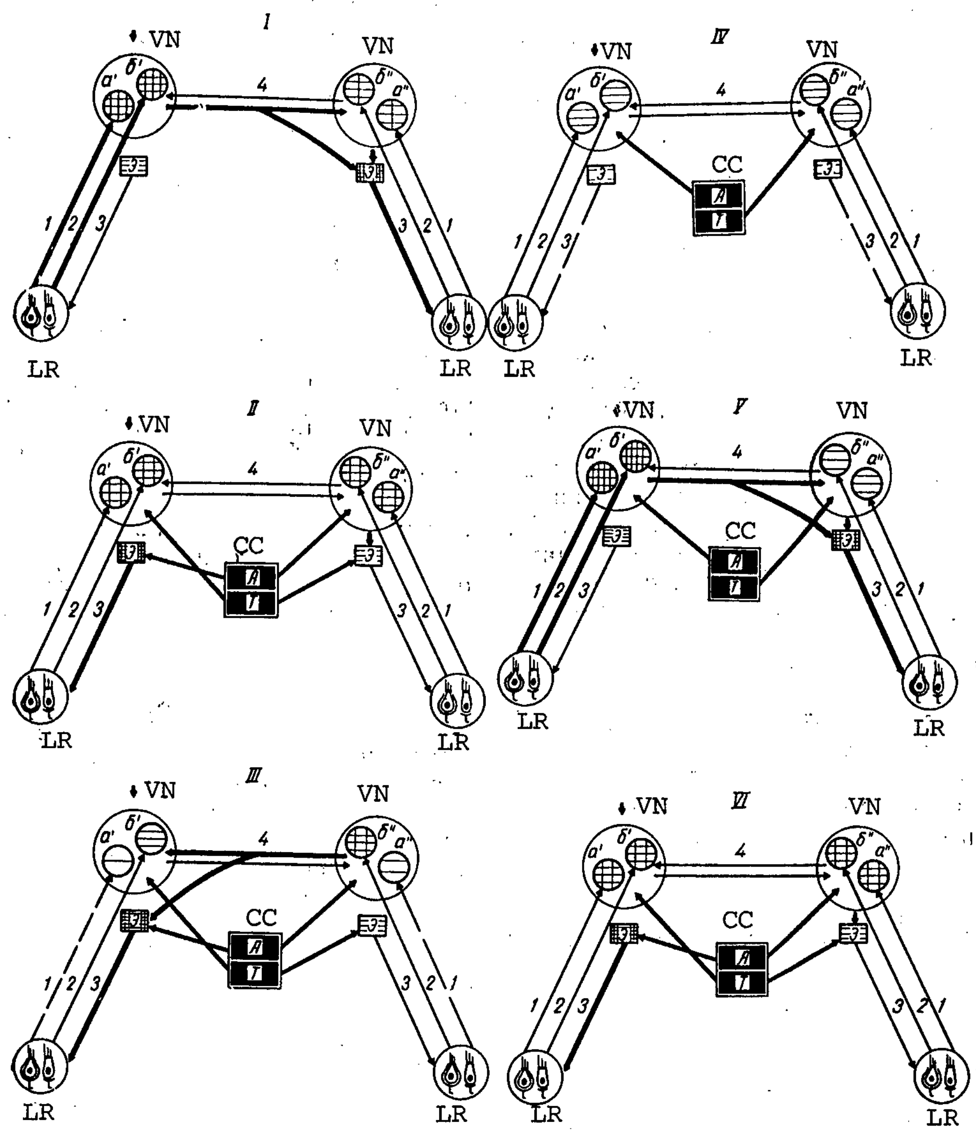

Figure 3. Hypothetical drawing that explains "baseline" uncompensated vestibular asymmetry (I), its compensation under normal conditions (II), appearance of vestibular asymmetry and its compensation in weightlessness (III and IV, respectively) and upon return to earth (V and VI, respectively)

a',b',a",b") neurons of vestibular nuclei
1,2) efferent connections of otolith system and semicircular canals, respectively, with vestibular nuclear neurons
3) afferent inhibitory connections with labyrinth receptors
4) bilateral, internuclear, commissural reciprocal connections
VN) vestibular nuclei
CC) compensating center
LR) labyrinthine receptors
A,T) activating and inhibiting zones of CC
э) nerve elements of VN, reticular formation of brain stem and cerebellum that initiate efferent nerve fibers

Level of activity of VN neurons and efferent nerve elements designated by number of horizontal and vertical lines. Vertical arrows show prevalence of extralabyrinthine excitatory influences on VN and efferent nerve elements. Boldface lines--intensification of corresponding influences, interrupted lines--weakly functioning connections

Otolith membrane weight loss in weightlessness leads to drastic decline of otolith afferentation [50, 88]. This would lead to decrease in background impulsation of corresponding nerve elements of vestibular nuclei. These changes probably develop immediately upon occurrence of weightlessness. Yet the compensating center, which was formed as a result of adaptive changes in the central nervous system in response to initial vestibular asymmetry, continues to function in the former "mode" in weightlessness. Since vestibular nuclei on the side of initial prevalence were more subject to inhibition and those on the contralateral side, to activation, a new internuclear imbalance appears, but with prevalence on the contralateral side (Figure 3,III). Depression of otolith afferentation on the side of original prevalence would be more marked, since there was more intensive descending inhibition on this side of labyrinthine receptors going via efferent fibers from neurons situated in the vestibular nuclear complex, reticular formation of the pons and medulla oblongata, and cerebellum [111, 112]. This probably explains appearance of asymmetry of otolith afferentation against the background of its decline, as demonstrated in experiments on frogs during orbital flight [88]. According to Baumgarten et al. [67, 68], appearance of otolith asymmetry was the cause of loop-like movements of fish with onset of weightlessness in parabolic and orbital flights.

Asymmetry of otolith afferentation would lead also to canal asymmetry. In this regard, we can refer to a recently published article [32], in which distinctly asymmetrical reactions of cervical muscles involved in onset of head jerking were recorded in pigeons with unilaterally severed saccular nerve in response to counterrotation at the same velocity, whereas change in spatial position of the head led to positional nystagmus. This phenomenon is based on the intimate anatomical and functional connections between the otolith and canal systems of the labyrinth on both the receptor level and the level of their central structures [63, 75, 79, 85, 86, 96, 97, 116]. Attenuation of proprioceptive afferentation may also be involved in development of canal asymmetry, since attenuation of proprioceptive afferentation of antigravity muscles is associated with significant changes in canal reactions [53, 102].

As we know, the effect of influence of the vestibular system on the central nervous system depends largely on imbalance of bioelectrical activity between vestibular nuclei on both sides [15, 17]. Investigation of morphological and functional organization of vestibular nuclei identified the mechanism, upon which this principle is based. In particular, at least two systems of communication between nuclear neurons and both labyrinths were demonstrated: reciprocally and synergistically organized connections. Postsynaptic inhibition, which is effected by commissural and internuncial neurons, is the main element of reciprocal internuclear correlations [15-19, 95, 101, 103, 118]. Asymmetrical vestibular reactions arise thanks to the reciprocally organized system of nuclear neuronal connections, while the synergistically organized system most probably provides for appearance of symmetrical vestibular reactions. Experimental studies revealed reciprocal correlations not only between vestibular nuclei, but between labyrinths on both sides. They are manifested by the fact that stimulation of receptors of one labyrinth is associated with inhibition of afferent activity of receptors of the contralateral labyrinth

[98, 114] which, in turn, leads to even greater internuclear imbalance. Thus, appearance of asymmetry on the level of the vestibular nuclei is one of the mandatory prerequisites for reactions that are adequate to stimulation. This was shown, in particular, by the studies of G. I. Gorgiladze [23] and Ye. B. Shulzhenko et al. [60]: passing descending direct current through both labyrinths, which created conditions that prevented development of internuclear vestibular asymmetry in response to a stimulus, made it difficult or even impossible for appropriate vestibular reactions to occur.

Under normal conditions, with appearance of vestibular internuclear asymmetry in response to a stimulus there is selective propagation of afferent impulses from labyrinthin receptors to the cerebral structures that transform them into sensory, autonomic and motor reactions that are adequate to the stimulus. Yet, when there is excessive asymmetry of afferentation from both labyrinths, such marked internuclear imbalance develops that existing regulatory mechanisms are inadequate, and instead of selective influence of impulsation from the vestibular system there is broad generalization of excitation over various cerebral elements, including the hypothalamus. As a result, sensory, motor and autonomic disturbances appear: sensations no longer correspond to reality, and they are manifested by vertigo and diverse illusions. The eyes do not track a target, nystagmus appears, etc. Such a state apparently is present when the function of one labyrinth is eliminated (for example, due to trauma and surgical intervention), as well as during attacks of Meniere's disease when there is an extremely asymmetrical flow of impulsation to vestibular nuclei. Apparently, in weightlessness vestibular asymmetry is not as marked as in the mentioned clinical cases. However, it is sufficient for afferent impulsation in response to ordinary stimuli to become generalized and cause a strong reaction. This probably explains why symptoms of motion sickness appear with head movement in the vast majority of cases. It may be that the nystagmoid eye movements observed in some cosmonauts during orbital flight and their obvious emphasis on one state at rest or with rotatory head movement were a manifestation of expressly vestibular asymmetry [2, 11].

One of the most typical distinctions of SMS is that its symptoms gradually regress and disappear within the first 3-5 days of orbital flight, after which they do not usually recur. Probably, such adaptation occurs due to certain changes in the compensating center, which cause attenuation of vestibular asymmetry that occurs in weightlessness (Figure 3,IV). In particular, they are manifested by restoration of otolith afferentation [88], which could be due to attenuation of activity of nerve elements that have a descending tonic inhibitory effect on labyrinthine receptors. The latter, as we know, is enhanced when there is increase in otolith and proprioceptive afferentation [75, 86, 96, 97, 116], and probably is attenuated when they are deficient in weightlessness. Evidently, development of adaptive changes is the explanation for increased resistance to motion sickness during interaction of Coriolis and precession accelerations, which was demonstrated in American astronauts on the 8th day of the orbital flight aboard the Skylab station [87].

The conception of impaired paired function of labyrinths under the effect of spaceflight factors explains the possibility of development of motion sickness, not only during orbital flight but in the recovery period of readjustment to

earth's gravity, as a result of continued function of the compensating center formed in weightlessness (Figure 3,V). The longer the spaceflights are, the more firmly "secured" the adaptive changes in the central nervous system caused by weightlessness, and apparently for this reason the incidence, as well as severity and duration of motion sickness and other symptoms of vestibular discomfort after spaceflights increase considerably with increase in flight duration [37, 61].

Vestibular asymmetry appears during spaceflights not only due to the direct effect of weightlessness on the vestibular input. Vestibular asymmetry (both peripheral and central) can appear also as a result of asymmetrical changes in blood and CSF [cerebrospinal fluid] circulation. According to studies pursued in weightlessness and after termination of long-term orbital flights, cosmonauts developed marked interhemisphere asymmetry of delivery of blood to cerebral vessels and signs of arterial and venous hypotension in the vertebrobasilar system [57, 62]. Yet it is known that relatively minor changes in blood pressure or blood flow in the internal auditory arteries often lead to vestibular dysfunction [121]. In the opinion of Cawthorne et al. [78] and according to the experimental data of Bodo et al. [6], systemic hemodynamic and neurohumoral changes are instrumental in appearance of vestibular asymmetry. Nor can we rule out the possibility of change in afferent activity of labyrinthine receptors as a result of some endolymphatic hypertension in weightlessness. When the shift of body fluids to the upper half of the body is reproduced in the laboratory using the head-down test to simulate weightlessness, elevation of fluid pressure was found in the inner ear, along with changes in receptor function of both the auditory and vestibular parts of the labyrinth. The demonstrated changes were usually asymmetrical, with prevalence of reaction on one side [106]. In view of the foregoing, it is important to stress that primarily unilateral hemodynamic and CSF disturbances in the labyrinths are among the prime causes of development of vestibular dysfunction in the presence of peripheral labyrinthine disease (vestibulopathy, sudden deafness, Meniere's disease and others) [31, 49, 55, 59]. Thus, in individuals suffering from unilateral Meniere's disease, distinct asymmetry of evoked vestibular reactions is demonstrable [3, 55]. Asymmetry appears due to areflexia on the involved side as a result of endolymphatic hydrops and, in all likelihood, it is the chief cause of vertigo, equilibrium disorders, spontaneous and positional nystagmus, nausea and vomiting in such patients. Yet removal of excessive endolymphatic fluid (intake of osmolytic agents, diverse types of decompressive surgical operations) leads to significant attenuation and even disappearance of manifestations of vestibular dysfunction [3], along with normalization of receptor function of the involved labyrinth and restoration of asymmetrical vestibular reactions. Spinal asymmetry, which was demonstrated in model experiments simulating some spaceflight factors, as well as significant intensification of interhemispheric asymmetry [39, 52], also constitute one of the causes of imbalance between paired vestibular structures, due to increased influx of asymmetrical impulsation to them [37]. It should also be noted that asymmetrical muscular contractions are associated with an increase in predisposition to experimentally evoked motion sickness [1].

The hypothesis on the role of vestibular asymmetry in the genesis of motion sickness is also confirmed by investigations pursued in the laboratory. Resistance to motion sickness was found to be considerably lower in individuals

with more or less noticeable baseline otolith asymmetry than without it [37]. Comparable results were obtained in the case of production of interlabyrinthine asymmetry by passing descending direct current through one labyrinth. This was associated with distinct decrease in tolerance to Coriolis and precession accelerations, which provoked motion sickness (Figure 4). According to the data of Ye. P. Maslova [46], canal asymmetry is significant in children, as compared to adults, apparently due to imperfection of compensatory mechanisms. At the same time, children were found to be considerably more susceptible to motion sickness [43]. Signs of vestibular dysfunction were demonstrated during clinostatic and particularly antiorthostatic [head-down tilt] hypokinesia or submersion in immersion medium. They were manifested the most distinctly by development of asymmetry of both canal and otolith reactions (see Figure 1) [37, 39, 53]. As we know, these methods of immobilization simulate at least three of the most important factors of spaceflight: hemodynamic changes in the form of redistribution of body fluids to the upper part of the body, proprioceptive deprivation as a result of removal of load on skeletomuscular system and restriction of motor activity, and finally changes in neurohumoral regulation leading to development of a general stress state [34, 39]. Each of these factors may be instrumental in appearance and intensification of vestibular asymmetry.

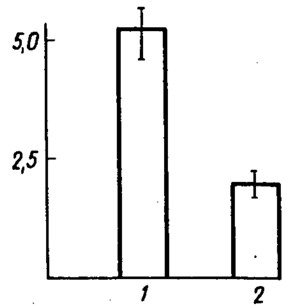

Figure 4.
Tolerance to test of I. I. Bryanov (in min) in normal state (1) and with delivery of descending direct current of 5.0 mA through right labyrinth (2)

There are some rather ambiguous data concerning the extent of baseline vestibular asymmetry in healthy people, ranging from virtually total absence to substantial variability. Moreover, this may be observed in the same subjects [4, 5, 25, 41, 44, 48, 64, 65, 77, 90, 93, 94, 108]. Such inconsistent demonstration of vestibular asymmetry under normal conditions probably reflects the dynamic state of the compensating center. It may be related to different causes: conditions under which test is performed, level of wakefulness, constant fluctuation of endogenous medium, exogenous stimuli. Thus, according to the results of studies we conducted on healthy subjects submitted for the first time to caloric stimulation of the labyrinths, there is reliable asymmetry of nystagmic reaction of the eyes, along with overt signs of stress (pallor of the face, perspiration, elevation of blood pressure, faster heart rate, in rare cases extrasystole). Apparently such stress is caused by the unfamiliar surroundings, application of electrodes, insertion of tubes in the auditory meatus, as well as warning the subjects that they could have unpleasant sensations when water is infused in the ear. Repeated testing of the same subjects 10-15 days later revealed symmetrical nystagmic reactions to the same caloric stimuli. The above-described symptoms of stress were also absent. In other studies, sleep deprivation led to considerable increase in asymmetry of spontaneous vestibular reactions in healthy individuals, as assessed with the step test [42]. Distinct asymmetry of vestibular responses was demonstrable in

individuals who were regularly exposed to noise and vibration [44, 48], as well as with such a strong stressor as Coriolis and precession accelerations that elicit motion sickness (see Figure 1) [37]. Practice flights, which present a considerable stress load for fighter pilots, were associated in some cases with onset of spontaneous nystagmus and heightened sensitivity to motion sickness [40]. According to data in [71, 72], vestibular (canal) asymmetry is the cause of diverse inflight illusions of motion in pilots. In the authors' opinion, flight conditions intensified baseline vestibular asymmetry, which led to spatial disorientation in the absence of visual information. It is also known that spontaneous nystagmus occurs in other functional tests, in particular with moderate hypoxia [117] and lower body negative pressure [10]. Another interesting phenomenon was discovered in the presence of stress factors, which consists of periodic alternation of direction of asymmetry of vestibular reactions [41, 48]. This phenomenon can be explained as follows: vestibular asymmetry can develop due to both impairment of established compensation and a sort of overcompensation, when vestibular nuclei originally having less activity prevail for a time over nuclei of the contralateral side.

There are several methods for demonstration of vestibular asymmetry. At first, the so-called "method of dual calorization" was proposed, which consisted of simultaneous irrigation of both auditory meatuses with water of the same temperature [113]. The author proceeded from the assumption that, under such conditions, nystagmus should be absent if there was identical excitability of both labyrinths. Yet, in the presence of a more or less noticeable baseline difference in their excitability, nystagmus will appear and will occur in a strictly specific direction, depending on water temperature and excitability of each labyrinth. This method did not gain recognition, since nystagmus and other vestibular reactions always appear in response to this method of stimulation of the labyrinths (in our terminology, "binaural equal calorization"), although they differ from those that occur with calorization of each labyrinth separately using water of the same temperature [20]. The method of bithermal calorization of labyrints gained the widest use for demonstration of canal asymmetry [82]: equal volumes of warm or cold water are alternately used to irrigate the meatuses for the same period of time, using a temperature that differs from body temperature by the same value (usually 30 and 44°C). In most cases, this method was used to stimulate the horizontal semicircular canals, and the subject's head would be placed in such a position as to have the canals directed vertically (head bent forward at an angle of 30° or backward at 60°). However, the existing facts indicate that other semicircular canals are also involved in the reaction with the head in such positions [20]. More recently, stop-stimulus and sinusoidal tests have been used [41, 48]. Sinusoidal rotation permits evaluation of asymmetry, not only according to time and amplitude characteristics of vestibular reactions, but phase relations between evoked reactions and the stimulus [41]. As a rule, to demonstrate otolith asymmetry the eyeball counterrotation reaction is measured by means of a successive visual image (indirect otolithometry method) [81] or by direct recording of movements of the eyeball proper (direct otolithometry) [84] with change in spatial position of the head (bending the body to both sides in the frontal plane). Finally, galvanization of labyrinths was used for demonstration of vestibular asymmetry. It does not have selective action with change in canal and otolith afferentation, and for this reason it permits evaluation of excitability of the labyrinth as a whole [15-18, 58, 107]. In most studies, vestibular asymmetry was demonstrated according to the oculomotor reaction (nystagmus and eyeball counterrotation reaction). Other

reactions (illusions, shift of general center of gravity of the body, gaze fixation) [25, 53] were used to a considerably lesser extent.

Development of vestibular asymmetry (both peripheral and central) under the effect of spaceflight factors is not the only possible mechanism of SMS pathogenesis. This hypothesis is not expounded as an alternative to other conceptions, in particular, the hypothesis of impaired integrative activity of the central nervous system or the hypothesis of sensory conflict as the prime cause of SMS [35, 36, 110]. As we know, formation of SMS has time-related dynamics. The receptors of the labyrinth, proprioceptors and some interoceptors "respond" to weightlessness virtually instantaneously, and they lead to development of vestibular asymmetry, just as they do to sensory conflict and change in customary pattern of visceral afferentation. However, at the very same time, certain changes start to take place in other organs and systems, and they reach a maximum after a significantly longer time. These changes are already the consequence of primary reactions caused by weightlessness. For example, redistribution of body fluids in a cranial direction elicits changes in blood and CSF dynamics, elevation of intracranial pressure and circulatory hypoxia of the brain due to venous stasis, change in fluid-electrolyte metabolism, circulating blood volume and neuroendocrine regulation [7, 8, 12, 27, 47]. All this can, of course, alter general reactivity, since it is a sort of critical background that lowers substantially the threshold of onset of motion sickness and, consequently, explains the established fact that SMS does not usually develop immediately after exposure to weightlessness, but considerably later (1 h to 1.5 days).

It should be stressed that B. B. Yegorov and G. I. Samarin [30] were the first, followed by Baumgarten et al. [69, 70], to mention the possibility of vestibular dysfunction during spaceflights as a result of development of interlabyrinthine, specifically otolith, asymmetry, on the basis of experiments on fish. At the same time, there is validation in this survey of the possibility of vestibular dysfunction under the effect of spaceflight factors, not only due to otolith, but canal, asymmetry, as well as changes in blood and CFS dynamics, stress and asymmetrical influx of extralabyrinthine signals to vestibular structures.

Thus, the material submitted in this survey indicates rather convincingly that there is a link between labyrinthine asymmetry and vestibular dysfunction. At the same time, further special-purpose investigations are needed in order to confirm the significance of this phenomenon to the genesis of SMS, and to use it as a prognostic test in cosmonaut screening. These investigations must include the following: evaluation of degree of otolith and canal asymmetry using various vestibulometric methods (otolithometry, bithermal calorization, sinusoidal rotation, electric stimulation of labyrinths and optokinetic tests) and recording the relevant motor, autonomic and sensory reactions under normal conditions and during various functional tests, use of stressors or simulation of spaceflight factors, particularly in actual flight; determination of vestibular asymmetry as a function of age, sex, occupation and constitutional distinctions of different individuals.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

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EVALUATION OF PHYSICAL WORK CAPACITY OF COSMONAUTS ABOARD SALYUT-6 STATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 17 Jun 85) pp 31-35

[Article by V. A. Tishler, A. V. Yeremin, V. I. Stepantsov and I. I. Funtova]

[English abstract from source] Electrocardiograms of Salyut-6 prime crewmembers recorded during their exercises on a bicycle ergometer and treadmill are presented. ECG were recorded by a portable tape recorder Cardiocassette and transmitted to the Earth via the radiocommunication channel. This procedure helped to better understand cardiovascular adaptation to different workloads, including submaximal, as well as reserve abilities of the body at various flight stages. This can be used advantageously to correct and control the training process as well as to predict the cardiovascular status at the final flight stage.

[Text] The specific living conditions aboard a spacecraft have a substantial influence on the condition of cosmonauts and could lead to decline of their physical work capacity, particularly in the case of long-term flights.

The system of preventive measures used in long-term manned flights [1] prevents to some extent the development of deconditioning of physiological systems, provided it is used regularly (onboard training equipment--treadmill--KTF [expansion unknown], bicycle ergometer, set of different expanders, myoelectrostimulation). It was deemed important to obtain objective information about the degree of change in physical performance in the course of training, in order to assess the functional capacities of cosmonauts, both during flight in order to make immediate corrections in the training method, and to predict the possible reactions of adaptation to earth's gravity in the early postflight days.

The method of testing inflight physical performance by means of analysis of physiological data received via telemetry during functional tests on cosmonauts with graded standard load on a bicycle ergometer can demonstrate only substantial deviations of adaptation to the load. However, minor deviations and early changes in work capacity are difficult to detect with this test, since the test load is relatively small (750 kg-m for 5 min). In addition,

there is habituation to ergometer loads performed by the cosmonauts daily during training. The radiotelemetry is also not always long enough, which makes it difficult to perform a comprehensive analysis of data received.

For this reason, a study was made of the possibility of obtaining and analyzing physiological information during performance of different types of physical exercises using onboard exercise equipment in order to detect the nuances in adaptation to loads differing in intensity in order to assess the physiological reserve capacities.

Methods

The ECG in the anterior Nehb lead was recorded on crews of three missions to the Salyut-6 orbital station, using a portable miniaturized tape recorder (Cardiocasette) which was secured on the subject's belt during exercise. The same recorder was used to reflect 28-s ECG segments as related to a specific load in verbal form. The ECG in the form of a frequency-modulated signal and verbal comments was then transmitted to earth over the radio communication channel and analyzed.

Concurrently with recording of the ECG, we recorded the training conditions (change in force, rate of movement, nature of load as to time) on a memory unit (MU). These data were than transmitted via the radiotelemetry channel to earth and analyzed together with the results of processing ECG's.

Results and Discussion

Table 1 lists data obtained during work on the ergometer by one of the crew members (K-3-1) of the third prime mission (EO-3) on Salyut-6. This table shows that his heart rate (HR) on the 84th day of flight changed in complete accordance with the force of exercise (only the second half of the training session was recorded).

The volume of all exercise done by K-3-1 on this day constituted 29,100 kg-m at a mean load rate of 800 kg-m/min. The physiological "cost" of this exercise did not reach high values, while the recovery rate was rather rapid, which was indicative of his high degree of conditioning at this stage of the flight. The ECG showed changes inherent in high load levels: shortening of all intervals, respiratory alternation of R waves, obliquely ascending shift in ST to 1.5 mm concurrently with decrease in PQ interval, some decline of R/T ratio due to increase in T wave. A typical distinction on the ECG of K-3-1 was early appearance of restitution (within 2-3 min) of marked respiratory arrhythmia (almost 2:1), which was also demonstrable after test loads. This apparently reflected the vagotonic nature of postload reactions, which is indicative of a high degree of conditioning.

Table 2 lists the dynamics of HR of K-3-1 on the 114th day of flight at the final stage of training.

A comparison to the preceding records shows somewhat greater HR reaction to a load of 950 kg-m/min. However, rapid recovery and adequate changes in ECG parameters do not allow us to assess this reaction as a decrease in work

capacity, particularly since the MU data were indicative of construction of this training on the principle of using large loads in the first half of the training period, which no doubt caused residual phenomena.

Table 1.
HR changes during exercise on bicycle ergometer on 84th flight day in K-3-1

Load intensity, kg-m/min	Exercise time, min	HR/min	Load intensity, kg-m/min	Exercise time, min	HR/min
850	1	126	1200	3	150
650	1	120	1050	3	162
950	3	138	rest	1	126
650	1	126	950	3	138
1050	4	144	rest	1	120
650	1	108	850	3	132
750	3	120	750	1	126
850	3	120	recovery		
950	1	138		1	96
Rest	1	120		2	80
1050	3	144		3	80
Rest	1	132		5	90

Table 2.
HR changes in K-3-1 during bicycle ergometer training on 114th flight day

Load intensity, kg-m/min	Exercise time, min	HR/min
750	5	120
Rest	1	84
750	3	120
650	1	114
850	3	138
Rest	1	78
950	3	168
Recovery	3	84

In the second cosmonaut (K-3-2), maximum HR on the 84th flight day during the functional test (750 kg-m/min, 5 min) constituted 102/min. There were minimal ECG changes. On the 112th day, in addition to data about the functional test, information was obtained about the end of the training, which revealed the following: HR constituted 114/min at a performance rate of 1200 kg-m/min (3 min), 132 at 650 kg-m/min (1 min), 144 at 1050 kg-m/min (3 min) and 138 at 750 kg-m/min (1 min). Even from this short record we see that higher load rates at the end of the training period were associated with relatively moderate HR changes. If we consider the total load of 34,200 kg-m and mean rate of 980 kg-m/min, we can say that K-3-2 had a high performance potential at this stage of flight.

Table 3 lists summary data referable to analysis of records from the MU and ECG at different stages of the flight of the fourth prime mission (EO-4). We were impressed by the substantial differences in load levels in crew members K-4-1 and K-4-2. The fact of the matter is that K-4-2, who had an extremely high baseline level of conditioning for endurance and good tolerance to the ergometer load, preferred expressly this mode of training and planned his exercise in such a way that the work load during the flight (according to records from the MU) was in the range of 35,000-48,700 kg-m, and while this parameter did not exceed 40,000 kg-m in the first half of the mission, it exceeded 43,000 kg-m in the second half.

Analysis of reactions to physical training during EO-4 revealed that they were adequate to the load on the 42d-45th day in both cosmonauts, and ECG parameters were normal and typical for the loads listed in Table 3. ECG tracings made on the same days on K-4-2 revealed that HR during run on the treadmill was 135-155/min in the moving mode and 150-160/min in the generator mode (motor

turned off, treadmill band moved by the action of the legs), which was also assessed as a rather satisfactory reaction.

Table 3. Summary data on volume, intensity and HR reactions when exercising on bicycle ergometer at different stages of EO-4 flight

Flight day	K-4-1			K-4-2		
	total training kg-m	mean intensity kg-m/min	maximum HR/min	total training kg-m	mean intensity kg-m/min	maximum HR/min
42—45	19600	750	143	36400	1100	155
70	21200	730	165	39600	1050	170
97	27800	960	165	43000	1130	170
135—134	26200	780	152	47000	1200	154
174	27300	880	140	45000	1150	150

On the 70th flight day, K-4-1 showed some increase in HR with moderate loads on the bicycle ergometer, up to 165/min, which served as grounds to assess his reaction as being associated with some strain on physiological systems involved in the exercise. True, the shape of the ECG did not reflect strained function, and it was consistent with the normal fluctuations of this HR. Analysis of information obtained on the 70th day during exercise on K-4-2 revealed that, in spite of use of moderate loads, HR rose to 170/min. This unusual reaction for him was assessed as manifestation of some strain on physiological systems. Apparently, this period (70th day) was associated with some processes that altered adequacy of responses. Analogous findings had been made on the 90th day of ground-based tests with long-term hypokinesia [2]. We cannot rule out the possibility of manifestation under such conditions of slow biological rhythms with a period of 70-90 days, and it is expressly at the end of this period that there is some decline of physiological reactions.

Prompt correction of loads resulted in finding that the HR reaction on the 97th flight day did not exceed former values, even with "peak" loads--1450 kg-m/min for K-4-1 and 1660 kg-m/min for K-4-2. The recovery period did not exceed 5 min for HR, while ECG parameters did not differ from the usual individual values.

The changes in ECG data while running in the same period confirmed the beneficial nature of adaptation to loads in both cosmonauts. Changes in load levels elicited an adequate HR reaction in K-4-1: during the difficult run in the generator mode for 1.5 min, this parameter reached 155/min, when running in the motor mode it was up to 150/min, and when changing to walking or strength-developing exercises HR dropped to 118-102/min. The ECG was characterized by the usual changes for such loads. In K-4-2, HR constituted 158-160/min during a 10-min run in generator mode at the rate of 150 steps/min (heavy exercise), with rapid recovery of parameters (by the 5th min).

Work on the bicycle ergometer was rather high in volume (26,200 kg-m) on the 135th day for K-4-1, and it was moderate in intensity (780 kg-m/min). There

were HR changes consistent with the load: 152/min with a peak load of 1250 kg-m/min, but it corresponded to the baseline by the end of the recovery period (5th min). The same HR pattern was observed during the run on the same day: HR rose to 125/min when running in motor mode at the rate of 160-170 steps/min for a "distance" of 1660 m, followed by rapid recovery of this parameter. In this period, the ECG changes did not differ from those inherent in this crew member.

On the 134th day, K-4-2 performed the flight's maximum exercise load (see Table 3), his HR was only 154/min with a load of 1660 kg-m/min, and came close to the baseline upon termination of exercise. This response and the moderate ECG changes indicate that K-4-2 had reached maximum work capacity at that time, as also confirmed by moderate changes in HR when working on KTF on the same day: when running in generator mode HR did not exceed 132/min and rapidly reverted to the baseline.

The last recording on the Cardiocasette of exercises was made on both crew members on the 174th day, shortly before the end of the mission. HR did not exceed 140/min in K-4-1 during exercise on the ergometer at high loads (see Table 3), which was indicative of his good adaptation to the physical load. For K-4-2, the ergometer load contined to be high, but his HR did not exceed 150/min at the "peak" load of 1500 kg-m/min for 5 min. There was a somewhat more pronounced HR reaction when working on the KTF (running in generator mode)--165/min.

Thus, it can be concluded that work capacity of the EO-4 crew during long-term exposure to flight factors not only failed to decline, but even grew in the second half of the mission as a result of regular physical conditioning by means of onboard exercise equipment. The period around the 70th day was an exception. HR changed during flight (as it did on the ground) in accordance with the load level. There was specific and, apparently, very rapid restitution of HR for the described conditions in the course of exercise and particularly after it. The mechanism of this phenomenon is not very clear as yet; it can be assumed that sympathovagal relations play a deciding role. We failed to observe instances of accumulation of fatigue in the course of individual exercise sessions, in spite of the fact that the work loads were rather high.

During the work of the fifth prime mission (EO-5) aboard Salyut-6, we obtained data about the training of the second cosmonaut (K-5-2).

On the 25th flight day, during work on the bicycle ergometer (total of 20,100 kg-m, mean intensity 950 kg-m/min) at load levels of 1000-1370 kg-m/min for 1.5-2 min each, HR was in the range of 125-148/min, which was assessed as an adequate response to a moderate load. We failed to demonstrate any distinctions in changes of ECG parameters. Conditioning on the KTF on the same day, two periods of running in the motor mode (5-10 min with a 6-min rest interval) caused HR to rise to 118/min, and recovery rate was rapid. ECG parameters did not differ from those recorded earlier on the same day.

The ECG tracings during exercise on the bicycle ergometer on the 42d day revealed that the load was substantially greater than on the 25th day (total

35,250 kg-m, mean intensity 880 kg-m/min), but nevertheless HR constituted 135-140/min at load levels of 1150-1250 kg-m/min, which was indicative of the fact that K-5-2 had achieved a good level of conditioning. There were no noticeable changes in the shape of the ECG.

As for crew member K-5-1, a tentative conclusion that he retained a high performance potential could be made on the basis of analysis of the structure and nature of training according to the MU records. Thus, on the 25th day his exercise volume was 35,000 kg-m at a mean intensity of 1000 kg-m/min, and he had worked at the rate of 1300-1500 kg-m/min continuously for 6 min, which can only be done by well-trained people. Similarly, he performed 5 runs on the KTF (total "distance" of about 6000 m) in 36 min, with 1-1.5-min intervals between them.

Thus, the results of testing physical work capacity during exercise using onboard equipment revealed the following.

The ECG tracing in the anterior lead of Nehb recorded on Cardiocassette tape during various types and intensities of exercise, correlated to the actual structure of training recorded in the MU provides us with an idea about the dynamics of adaptation of the cardiovascular system to different, including submaximum, loads, as well as reserve capacities of the body at different stages of flight. Such information is extremely important to evaluation of current status of the crew, particularly when planning high-load elements in the flight program (for example, extravehicular activity), as well as to predict their status at the final stage of flight. In addition, this information makes it possible to immediately correct elements of the training process if necessary, i.e., to control it judiciously.

The system of preventive measures, in particular physical exercise, is an effective means of maintaining physical work capacity during flights, provided it is practiced regularly to an extent that is adequate for shifting body functions from a state of equilibrium far beyond the resting level [3-5]. In this case, not only is it possible to preserve work capacity at its baseline level, to but increase it to the range required to perform unplanned operations (repairs in open space and others).

Analysis of the ECG and records of exercise structure on the MU during 3 expeditions to the Salyut-6 station indicates that there were good adaptive responses to different physical loads in all crew members.

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OPERATOR WORK CAPACITY IN TRACKING SYSTEM WHEN SUBMITTED TO ANTIORTHOSTATIC HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 5 Apr 85) pp 36-39

[Article by L. S. Khachaturyants† and A. K. Yepishkin]

[English abstract from source] It is shown that the work capacity of head-down tilted operators performing sensorimotor pursuit depends on their CNS state. The operators who react to the exposure showing moderate predominance of excitation processes display best work capacity.

[Text] Antiorthostatic [head-down tilt] hypokinesia (HDT) is one of the most widely used methods of simulating the effects of spaceflight factors related to redistribution of body fluids. As a result of numerous investigations, changes in biochemical processes, disturbances referable to the cardiovascular, respiratory, muscular and other physiological systems inherent in the "acute" period of adaptation to weightlessness have been studied rather fully [7, 10, 11, 15].

There has been considerably less investigation of the question of operator performance under HDT conditions, and the existing data concerning the extent of changes are contradictory in some cases [2, 4, 8, 14]. Our objective here was to examine the effect of HDT on operator work capacity when performing sensorimotor tracking. The choice of this type of work was based on the fact that tracking plays the leading role in most control systems.

Methods

Relatively strict 56-h HDT at an angle of -10 to -15° was simulated (Footnote 1) (Simulation of HDT was performed by V. A. Degtyarev and associates). Throughout the test period, the subjects remained supine, turning to their side or on their abdomen only periodically (during intake of food, personal hygiene).

Sensorimotor tracking was performed on an ERPS instrument (electronic recorder of tracking processes), which constituted an achievement test of two-coordinate tracking of a photic stimulus [5]. The screen of the instrument (a cathode-ray tube) was in front of the operator's face at a distance of 50-60 cm. The unit with the control knob was portable, so that it could be placed in any convenient

place without impairing the HDT position. The task for the subjects was to track the light signal which moved in a circle on the ELT [cathode-ray tube] screen at the rate of 50 angular min/s with a spot finder using the control knob. Tracking was effected in three work modes: 1) with uniform movement of the marker over the circumference; 2) with addition of an inertial link in the control chain (time constant τ_3 = 1 s) and 3) complicated (sinusoidal) form of spot-marker movement. Each of the three programs was delivered for 5 min.

The quality of performance was evaluated by the modulus of the vector of stimulus and finder mismatch, which was inputted on a PS-100 calculator in pulsed form for a constant work time (100 s). Readings were made from the calculator every 10 s.

In addition, we tested the subjects' motor reaction to sensory (photic and audio) stimuli, and accuracy of reproducing intervals of 0.5, 1, 2, 3 and 6 s (Time method). When instructed by the experimenter, the subjects "closed" a radiotelegraph key for a specific time. Each interval was repeated 5 times per session in random order. We calculated the mean relative error of reproduction using the following formula:

$$\underline{M} = \frac{\underline{T_s} - \underline{T_o}}{\underline{T_o}}$$

where M is relative mean error, T_s is time of subjective reproduction of exposed time and T_o is objective duration of exposed interval.

In the course of a 56-h test, there were 16 work sessions with each operator on the ERPS instrument, 12 by the Time method and 12 measurements of sensorimotor reaction time.

In all there were 12 investigations involving 12 male subjects 18 to 34 years of age, who presented no deviations of health status.

We held preliminary practice sessions with the subjects, which involved two stages; the first was to acquaint them with the conditions and work in seated position, the second was work in horizontal position with the head end of the table slightly elevated (6-10°) in order to develop a firm skill in working while reclining.

The obtained data were submitted to statistical processing by conventional methods, with determination of arithmetic means (M), their dispersion (σ) and arithmetic mean errors (m). Reliability was determined using Student's t criterion.

Results and Discussion

Table 1 lists the results of testing work capacity.

The table shows that changes in quality characteristics of operator performance under HDT conditions were in a rather broad range. Thus, error of sensorimotor tracking could increase 2-5-fold or more and sensorimotor reaction time varied from 6 to 32%, whereas accuracy of reproducing time intervals changed in the direction of both exaggeration and underestimation.

Table 1. Qualitative characteristics of operator performance under HDT conditions

Type of activity	Parameter measured	Baseline	HDT
Sensorimotor pursuit tracking			
Work mode: I	Mismatch error, arbitrary units	23	50-120
II		34	75-158
III		42	87-220
Simple motor reactions to sensory signals: photic	Time, ms	210	235-270
audio		180	190-238
Reproduction of specified intervals	Relative error, arbitrary units	-0.2-+0.3	-0.7-+0.95

Of course, individual distinctions of operators and their psychophysiological reaction to simulated working conditions were the cause of such scatter in performance results. Demonstration of these distinctions was possible due to analysis of precision characteristics of reproducing specified intervals, since changes in parameters of sensorimotor function of operators were in the same directions.

Authors who have tested human capacity to gage time intervals relate it primarily to the condition of the central nervous system and balance between inhibitory and excitatory processes [3, 6, 12, 13, 16, 17]. There is subjective increase in gaged time in the case of prevalence of excitatory processes and slowing with prevalence of inhibitory processes.

According to Yu. M. Zabrodin et al. [9], processes of reflecting time change in the direction of exaggeration under extreme (stress) conditions, although the sign of the error may be either a plus or minus under ordinary conditions.

In our investigations, baseline testing of operators also separated them into three analogous groups: those who uderestimated exposed intervals (group 1), those who exaggerated them (group 2) and those who gaged them correctly (group 3). Under HDT conditions, this tendency changed reliably ($P<0.05$) in both the direction of further underestimation and exaggeration of intervals. In groups 2 and 3, the magnitude of change and the direction varied, so that they could be further separated into two subgroups (a and b). Such distribution of operators according to their capacity to gage intervals enabled us to compare this psychophysiological parameter to the quality of performance of sensorimotor operations (Table 2).

The data listed in this table indicate that in group 1 operators there was even greater further underestimation of exposed intervals during HDT. This group is characterized also by the lowest results of performance in the system of sensorimotor tracking in all three work modes.

A poor quality of performance was also noted in group 2a operators, who overestimated the time segments in baseline tests with retention of this tendency during the investigation.

Table 2. Comparative characteristics of results of operator performance with HDT (M±σ)

Group	HDT					
	gaging intervals	sensorimotor tracking			motor reaction	
		work mode			photic signal	audio signal
		I	II	III		
1	—0,6±0,02	105±5,2	144±5,8	210±5,6	229±8,4	262±5,5
2a	+0,87±0,01	100±5,6	159±5,3	198±7,9	220±7,9	251±6,1
2b	+0,05±0,1	80±5,3	96±5,7	150±5,4	216±8,1	243±5,9
3a	—0,08±0,02	77±5,7	88±5,2	120±6,2	209±8,5	244±6,3
3b	+0,06±0,02	64±5,1	82±5,4	95±7,1	199±8,4	241±6,3

Performance was better in operators who overestimated the exposed intervals in baseline tests but relatively underestimated them (coming close to the actual duration) under HDT conditions (group 2b); this also applies to group 3a who accurately measured intervals under baseline conditions with some underestimation with HDT.

Lowest tracking results (lowest mismatch error [sic]) were found in group 3b who accurately gaged the intervals with a tendency toward relative overestimation in the course of the study.

An analogous correlation was noted when we analyzed the simple sensorimotor reaction to a sensory stimulus: there was the greatest increase in reaction time in groups 1 and 2a, and the least in group 3b.

This was less marked than the relations in sensorimotor tracking, and it is attributable to the fact that a simple motor reaction does not require any complicated mental activity by the individual.

On the basis of the theoretical premise that there is a link between precision of reproduction of time intervals and condition of the central nervous system, it can be considered that, in group 1 operators submitted to HDT, there is buildup of inhibitory processes and their significant prevalence over excitatory ones. In groups 2 and 3, the change may occur in two directions: prevalence of excitation or inhibition. And, as we see, buildup of inhibition and significant excitation has an adverse effect on operator performance in a system of sensorimotor tracking. This is particularly vivid when the work is more complicated. Thus, addition of an inertial element in the control system (mode II) leads to noticeable worsening of performance, primarily in group 2a operators, in whom the excitatory process is considerably stronger than the inhibitory one. When, however, working in the mode with complicated form of movement of a marker-signal light (mode III), poorest results are observed in group 1 operators who have prevalence of inhibitory processes. They clearly present delayed reactions to change in movement of the marker on the ELT screen.

It should be assumed that the individual differences demonstrated in the course of these investigation in reactions of subjects submitted to HDT were the cause of differences in interpretation of results of previous work done in

this direction. Thus, data have been reported [1, 2] of heightened excitability of the central nervous system with a corresponding increase in amplitude and oscillations of β-waves on the EEG of an individual submitted to HDT, whereas elsewhere [11], it is reported, on the contrary, that there was decline of tonus and function of the cerebral cortex with increase in number of slow waves and decrease in β activity on the EEG.

The results of these investigations indicate that with HDT the central nervous system may change in both the direction of increased and decreased excitability, depending on individual distinctions of operators, which is consistent to some extent with the data obtained by A. A. Leonov and V. I. Lebedev [12]. However, we were unable to demonstrate a relationship between accuracy of gaging time intervals and the operators' general condition as had been done by the cited authors, perhaps due to the limited volume of tests. The cited authors, however, on the basis of 87 tests, established that poor tolerance to short-term weightlessness corresponds to subjective underestimation of passage of time, while good tolerance corresponds to proper or overestimated gaging.

Thus, the studies revealed that the success of operator performance in a tracking system when submitted to HDT is largely determined by individual psychophysiological reactions to the simulated conditions. In particular, it depends on the condition of the central nervous system (balance between inhibitory and excitatory processes) which, according to the teaching of I. P. Pavlov, is at the basis of all behavioral reactions of an individual. Best results were obtained for operators who reacted with moderate prevalence of excitatory processes.

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BLOOD LIPIDS AND INCIDENCE OF LIPEMIA IN FLIGHT PERSONNEL

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 16 Jul 85) pp 39-43

[Article by S. A. Bugrov, R. K. Kiselev, R. V. Beleda, V. I. Plakhatnyuk, N. N. Artamonov, A. P. Ivanchikov and V. A. Tsyganok]

[English abstract from source] The content of cholesterol and triglycerides was measured in healthy pilots. Over 1500 subjects were examined and age-related norms of the parameter were established. They were compared with published data. Physiological variations of cholesterol and triglycerides were related to age, height and body weight. The authors developed a method for diagnosing hyperlipidemia based on the agreement or disagreement between experimentally measured and theoretically calculated values. The authors maintain that hyperlipidemia can be diagnosed if the difference between the real and expected values is over 10%. The authors calculated the incidence of hyperlipidemia in all subjects examined (over 2100) and found that it was high: even in pilots of the age group 20-29 years hyperlipidemia occurred in 30% of the subjects.

[Text] In determining the nature of cardiovascular pathology, in most cases [7, 10, 13, 15, 19] researchers try to establish the role of risk factors, including the one for lipemia, in onset of these diseases. The existing clinical and epidemiological facts convince us that lipemia, which is associated with increase in blood atherogenic lipoprotein (LP) content, is one of the prime causes of development of atherosclerosis and ischemic heart disease, and that it is in first place among endogenous risk factors for this pathology [9].

Lipemia can be diagnosed provided one has knowledge of the physiological standards for lipid parameters differentiated according to age. A number of works by Soviet [4, 11] and foreign [14, 16, 17] researchers deal with this question, but they concentrated on older age groups.

We discuss here data concerning cholesterol and triglyceride levels in healthy flight personnel according to age groups, as well as incidence of lipemia in this contingent.

Methods

These studies were conducted with the participation of flight personnel who underwent examination and certification by a medical flight commission under clinical conditions in connection with a routine check, as well as after various diseases or when returning to flying work. In all, 2186 people were examined ranging in age from 18 to 53 years. The group formed in order to elaborate norms for blood lipids consisted only of individuals who were deemed healthy by the expert medical commission for flight personnel or else had diseases unrelated to function of the cardiovascular system. The subjects were divided into age groups (5-year increments). Since the groups for those under 20 and over 50 years of age were small, the data for them are not reported here.

Fasting blood was drawn in the morning. Lipids were assayed in serum using the Biotest-Lakhema sets (CSSR): cholesterol was assayed by the direct method with 2,5-dimethylbenzene sulfonic acid in the presence of sulfuric acid and triglycerides, by the reaction of formaldehyde with acetyl acetone (triolein served as the standard).

The material was submitted to statistical processing.

Results and Discussion

Physiologically differentiated norms for blood lipids were derived from the results of biochemical analysis of lipids in the group of healthy flight personnel, and they are listed in Table 1. We were impressed by the fact that cholesterol and triglyceride levels rose with age, which is consistent with data in the literature [13, 19]. However, the rate of cholesterol and triglyceride increment was not the same in the different age groups. Cholesterol increment in 5-year segments was about the same (0.34-0.39 mmol/ℓ). The minimal increment of cholesterol is observed between 35 and 40 years of age (0.10 mmol/ℓ). Increment of triglycerides constituted a mean of 0.10-0.18 mmol/ℓ, and minimal increment was observed in the 30-34 year group. Since there were more than 100 cases in each age group, and 300 or more for cholesterol in the groups from 25 to 39 years, it can be maintained with a high degree of probability that the results reflect the actual state of lipid metabolism in flight personnel.

Table 1. Physiological norms for blood lipids of healthy flight personnel differentiated according to age

Blood lipids	Statistical parameter	Age group, years					
		20—24	25—29	30—34	35—39	40—44	45—49
Cholesterol, mmol/ℓ	$\overline{X}$	4,59	4,95	5,29	5,39	5,78	6,06
	σ	0,90	1,06	1,06	1,10	1,21	0,98
	m	0,07	0,09	0,05	0,10	0,11	0,09
	n	229	316	392	298	188	166
Triglycerides, mmol/ℓ	$\overline{X}$	1,45	1,55	1,58	1,76	1,88	1,96
	σ	0,53	0,65	0,65	0,64	0,68	0,83
	m	0,04	0,06	0,03	0,06	0,06	0,07
	n	167	138	405	116	112	128

Table 2. Blood lipid levels in healthy flight personnel as compared to data in the literature ($\overline{X}$)

Blood lipids	Reference	Age group, years								
		20–24	20–29	25–29	30–34	30–39	35–39	40–44	40–49	45–49
Cholesterol, mmol/ℓ	[4]		5,83			6,16			6,53	
	[14]		5,42			6,19			6,70	
	[16]	4,62		5,03	5,52		5,57	5,91		6,14
	[17]	4,73		4,91	4,84		5,04		5,09	
	[11]							5,68		5,75
	Our data	4,59		4,95	5,29		5,39	5,78		6,06
Triglycerides mmol/ℓ	[4]		1,83			2,21			2,71	
	[14]		2,36			2,95			3,54	
	[17]	1,30		1,21	1,41		1,22		1,15	
	[11]							1,38		1,39
	Our data	1,45		1,55	1,58		1,76	1,88		1,96

A comparison of our findings with the data of other authors (Table 2) shows that cholesterol levels in healthy flight personnel were somewhat lower in the late 1970's and early 1980's than in the late 1960's. These minor differences could be attributed to the fact that results were obtained using different methods of analyzing blood lipids. Our data conform well with those for cholesterol and triglyceride levels in flight personnel of the GDR Air Force [17] for young age groups. For groups over 30 years of age, the data of B. Jarsumbeck et al. [16] are 0.5-1.0 mmol/ℓ lower for both parameters. This apparently indicates that aviation physicians and flight personnel themselves devote much attention to blood lipid levels and use preventive measures to keep them at optimum values.

For the group in the 5th decade, our data were close to those obtained by the All-Union Cardiological Research Center, USSR Academy of Medical Sciences, under the supervision of Ye. I. Chazov [11]. This enables us to expound the hypothesis that cholesterol levels in flight personnel referable to these age groups do not differ appreciably from those found in a screening of the male population of Moscow and Leningrad. The differences in triglyceride levels are perhaps related to use of different standards. Our findings coincide well with data in [16], which were obtained using the direct method of cholesterol testing.

Considerable differences (1.0 mmol/ℓ or more) were observed in comparison to data in [4] and [14]. Those reported in [6] were obtained for donors who gave blood postprandially, which leads to overestimation of all lipid parameters, particularly triglycerides. The differences from data cited in [14] may be indicative of qualitatively different standard of living and diet, as compared to ours, or other factors.

Knowledge of physiological differentiated norms for blood lipids also enables us to solve the following problem, diagnosing lipemia as the prime endogenous risk factor for development of cardiovascular atherogenic diseases. This

problem can be resolved in two directions: a) use of an arbitrary top range for each parameter, b) determination of consistency between actual and nominal blood lipid values. The following arbitrary top values have been adopted for all age groups over 30 years in the USSR on the basis of results of joint Soviet-American investigations [11]: for cholesterol 6.45 mmol/ℓ (250 mg%) and for triglycerides 1.58 mmol/ℓ. This approach is simple and convenient; however, it does not take into consideration the differentiated standard according to age and is recommended for older age groups, whereas lipemia is also observed in young people. The other approach, determination of consistency between actual and nominal values for blood lipids, does not have these flaws in our opinion.

The concept of nominal values for parameters that are a close correlative function of age, anthropometric data and other most constant characteristics of the body has been gaining increasing popularity in medicine in recent times [1, 12, 18, 20]. Knowledge of nominal values helps assess the accuracy of obtained or measured results, as well as extent of deviation from the physiological norm. As a rule, nominal values are determined by calculation or with the help of nomograms.

Calculation was made of equations of linear regression on the basis of analysis of cholesterol and triglyceride levels in healthy flight personnel, which enable us to determine nominal values for these lipids according to data on height, age and weight.

Table 3.
Incidence of lipemia (%) among flight personnel

Age group, years	Cholesterol	Tri-glycerides
20—24	28,9 (207)	32,4 (111)
25—29	31,7 (408)	32,1 (244)
30—34	35,8 (520)	40,8 (333)
35—39	33,4 (577)	48,0 (281)
40—44	35,6 (233)	46,4 (153)
45—49	33,2 (241)	43,6 (195)

Note: Number of subjects given in parentheses.

In these studies, it was shown that actual lipid levels in healthy man correspond well to nominal values, and the observed differences never exceeded 10%. In the group with atherogenic cardiovascular disease, these differences were always greater for the two parameters. The findings made it possible to expound the hypothesis that lipemia can be diagnosed when differences between actual and nominal lipid values exceed 10%. This approach made it possible to detect "milder" forms of lipemia and to do so at earlier stages of its development. The incidence of lipemia among all of the flight personnel surveyed was calculated using the methodological approach we developed for detection of lipemia from the standpoint of agreement between actual and nominal values. The results (Table 3) indicate that the incidence of lipemia is rather high: it is encountered in one-third of the flight personnel 20 to 29 years of age. In the most productive period of their flying career, 30-40 years, hypertriglyceridemia is demonstrable in almost half of the contingent studied.

The data we obtained on incidence of lipemia in flight personnel are not in contradiction with those in the literature. Thus, hypercholesterolemia in flight personnel was diagnosed in 36% according to [3] and in 75% according

to [5] (at the age of 45-55 years). The authors of the cited references were governed by the thesis of A. L. Myasnikov [8], according to which all cases of cholesterol levels in excess of 200-220 mg% are considered to be hypercholesterolemia. Such different figures for incidence of hypercholesterolemia are indicative of the importance of defining the lipid levels above which it is possible to diagnose lipemia.

Prompt detection of lipemia and institution of preventive steps should be one of the pressing tasks facing aviation physicians, since the risk of development of atherogenic cardiovascular disease is high for this group. A regular work and rest schedule, reasonable planning of flight load and increased exercise should help normalize lipid metabolism, particularly in young people [2, 6]. In some cases, one can use an altered diet and pharmacological agents.

Thus, the proposed method of diagnosing lipemia on the basis of discrepancy between actual and nominal blood lipid levels can be used in the system of medical observation of flight personnel for the purpose of early detection of this condition and institution of preventive measures to extend longevity in flight work.

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LINK BETWEEN ASYMMETRY OF OPTOKINETIC NYSTAGMUS, OPTOVESTIBULAR AND VESTIBULOVEGETATIVE STABILITY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 29 Apr 85) pp 43-45

[Article by V. K. Grigorova (People's Republic of Bulgaria)]

[English abstract from source] Comparative quantitative analysis of physiological asymmetry of the optokinetic nystagmus produced predominantly by central optokinetic stimulation (field of vision = 30°) or peripheral stimulation (field of vision = 110°) reveals an objective correlation between the asymmetry coefficient of the central optokinetic nystagmus with respect to the angular velocity of its slow phase and susceptibility to motion sickness caused by Coriolis and pseudo-Coriolis acceleration, the nystagmus velocity being up to 45 deg/sec.

[Text] It is known that many symptoms of motion sickness (MS) are similar to those of central and peripheral disturbances in the vestibular system. Asymmetry of nystagmic reactions is often the most important indicator in the diagnosis of such disturbances. For this reason, we decided to explore the informativeness of asymmetry of optokinetic nystagmus (OKN) for prediction of vestibulovegetative and optovestibular stability of healthy individuals [2].

Methods

We screened 60 healthy individuals 20-45 years of age without subjective or objective deviations referable to visual, vestibular and acoustic systems. Two series of studies were pursued.

In series I there were 30 participants whose tolerance to motion sickness was determined by the method of pseudo-Coriolis accelerations after [4]. Optokinetic stimulation (OKS) with the head inclined to the right and left shoulder lasted 10 min. Subjects who had autonomic reactions (AR) with grade 0 to OKS constituted group 1_I--optovestibular stability, while those who developed grade I or II AR made up group 2_I--optovestibular instability.

OKS was produced with either a television or optokinetic stimulator, on the screen of which were projected vertical black and white bands, with a width of 3 angular degrees that moved horizontally; the distance between the screen

and subject was 85 cm, field of vision horizontally 30°; or else a revolving optokinetic cylinder with vertical black and white bands 8° wide were used, and then the distance between the subject and screen was 140 cm, and horizontal visual field was 110°.

At first, all subjects were submitted to OKS at 5 velocities (4, 14, 29, 45 and 65°/s) in both directions. Then 15 subjects were submitted to OKS at 8 velocities (4, 14, 17, 22, 25, 29, 36-38, 45-50°/s).

In series II, we tested 30 individuals who did not participate in the first one. Vestibulovegetative stability (VVS) was determined using the test of I. I. Bryanov [1]. The subjects were divided into 3 groups according to intensity of AR and test endurance time: group 1_{II} consisted of highly stable subjects who endured a 10-min test without MS symptoms; group 2_{II} consisted of those who presented MS symptoms in the 4th-10th min of rotation, and group 3_{II} consisted of subjects who were unstable and developed MS in less than 4 min of rotation. OKN was induced by television OKS at velocities of 4, 14, 29, 45 and 65°/s in both directions.

During OKS, the subjects in both series were to watch the screen attentively, mentally count each black band passing through the center of the screen without tracking it further.

The nystagmographic method was used to record horizontal OKN. Asymmetry of OKN was assessed according to angular velocity of its slow phase (mean of 10 successive nystagmic jerks at the peak of the response after achievement of constant OKS velocity) and frequency of OKN (mean over 10 s at peak reaction time).

Asymmetry was expressed for each subject as the ratio of difference in values for parameters of OKN directed to the right and left to their sum.

Results and Discussion

In spite of the existing opinion [3, 5, 6], we believe that one can induce two types of horizontal OKN in man: central and peripheral. The size of the visual field included in OKS is the deciding factor in the type of OKN. OKN caused by televsion OKS (covering a field of 30°) was called central [4, 7] and that elicited by the optokinetic cylinder, peripheral (110° coverage of visual field).

Table 1 lists the coefficients of OKN asymmetry according to angular velocity of slow phase of central and peripheral OKN for subjects in group 1_I (20 people) and 2_I (10 people). As we see, the coefficient of central OKN asymmetry is higher in group 2_I than group 1_I (at OKS velocity of 45°/s; $P<0.02$). The coefficient of central OKN asymmetry is higher than that of peripheral, and this is reliable for group 1_I ($P<0.01$) starting at a velocity of 45°/s, and for group 2_I starting at 29°/s ($P<0.001$). In order to confirm these findings, we increased OKS velocities to 8, and 15 subjects (9 in group 1_I and 6 in group 2_I) were retested. Results of analysis revealed that statistically significant differences between coefficients of central and peripheral OKN asymmetry were observed at OKS velocity of 22°/s for group 2_I ($P<0.01$) and 36-38°/s for group 1_I ($P<0.045$).

Table 1. Coefficients of asymmetry of angular velocity of slow phase of OKN (M±m)

Angular velocity of OKS, °/s	Group 1_I		Group 2_I	
	central OKN	peripheral OKN	central OKN	peripheral OKN
4	14,7±1,9	16,1±3,6	17,2±2,5	25,2±6,3
14	9,3±1,88	11,3±2,5	12,5±2,7	8,3±2,0
29	11,9±2,5	7,3±1,6	19,7±3,9	5,2±1,4**
45	15,7±1,96	6,2±1,3*	30,4±5,8	4,9±1,0**
65	22,3±3,91	5,2±1,16**	28,0±5,8	4,6±1,4**

*$P<0,01$.
**$P<0,001$.

Table 2.
Coefficients of asymmetry of angular velocity of slow phase of central OKN in subjects differing in vestibulovegetative stability (M±m)

Angular velocity OKS, °/s	Group		
	1_{II}	2_{II}	3_{III}
4	21,1±5,4	24,5±5,5	16,3±3,7
14	10,4±2,4	10,0±3,3	11,2±2,2
29	8,1±1,95	12,3±2,9	17,7±4,4
45	11,5±2,2	10,5±3,6	32,3±5,1*
65	18,9±3,8	21,9±2,6	33,9±6,8

*$P<0,01$.

Analysis of coefficient of OKN frequency asymmetry failed to demonstrate statistically significant differences between the two types of OKN, or between subjects in groups 1_I and 2_I.

Table 2 lists the results of analysis of coefficients of asymmetry of OKN angular velocity in the slow phase for series II investigations. The mean values for the asymmetry coefficient are lower in groups 1_{II} and 2_{II} than group 3_{II}, and this difference is statistically significant ($P<0.01$) at OKS velocity of 45°/s. This coincides with the results in the first series of investigations. The absence of statistical difference between asymmetry coefficients in groups 1_I and 2_I, and groups 1_{II}, 2_{II} and 3_{II} at OKS velocity of 65°/s is most probably attributable to the fact that, in most subjects (particularly those in groups 2_I and 3_{II}), there is no central OKN at this velocity, or else it is irregular, which makes it difficult to evaluate quantitatively.

No statistically significant differences were demonstrated between coefficients for asymmetry of OKN frequency in subjects differing in vestibulovegetative stability.

Our results are indicative of an objective link between coefficient of asymmetry of velocity of slow phase of central OKN and man's tolerance to MS induced by Coriolis or pseudo-Coriolis accelerations. OKN asymmetry is related mainly to central cerebral structures and cerebral cortex that are importantly involved in formation of the symptoms of motion sickness. On this basis, it should be assumed that the demonstrated link is not a chance finding.

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PHYSIOLOGICAL MECHANISMS LIMITING EXTERNAL RESISTANCE TO RESPIRATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by M. A. Tikhonov and N. M. Asyamolova]

[English abstract from source] A study was performed on 8 healthy male subjects to investigate the effect of nonelastic resistance 6-40 GPa (the air flow velocity being 90 l/min) on the duration of proprioceptive reflexes of respiratory muscles, volume and velocity parameters of forced exhalation. Resistance of 15 and 25 GPa combined with a workload of 100-150 W increased the duration of proprioceptive reflexes from 0.18±0.015 to 0.29±0.012 sec and to 0.38±0.06 sec, respectively, which indicates fatigues of respiratory muscles. Resistance of 25 GPa reduced significantly (by 55%) the maximum volume velocity of forced exhalation and increased its duration by 31%, the exhalation volume decreasing insignificantly (by 6%). The major factor limiting man's tolerance to external respiration resistance is functional deficiency of proprioceptive regulation of respiration and strength and velocity of respiratory muscles.

[Text] To date, the time, velocity and volumetric distinctions of the respiratory pattern with external resistance have been investigated rather comprehensively [1, 5, 8, 10]. Many of these distinctions are being interpreted successfully from the standpoint of the rather fruitful conception of respiratory regulation for "perturbation" proposed by L. L. Shik [6]. This conception implies the priority of neuroreflex influences on the structure of respiration in the presence of exogenous resistance and a physical load. However, there has not yet been sufficient experimental confirmation of this priority.

We describe here a study of the role of proprioceptive regulation of respiration and velocity-force characteristics of respiratory muscles in the physiological mechanisms that limit human tolerance to exogenous resistance to respiration at rest and during exercise.

Methods

In our studies, which involved participation of 8 essentially healthy men 18-23 years of age, we investigated the time characteristics of proprioceptive

reflexes of respiratory muscles by means of abrupt blocking of air flow with a pneumatic valve installed on a Fleisch type pneumotachographic tube. The reflex was timed from the start of blocking air flow recorded on the pneumotachogram to appearance of an extra wave on the curve of mouthpiece pressure, which reflects appearance of additional inspiratory or expiratory exertion developed by respiratory muscles to overcome the suddenly appearing obstacle to respiration. This is the time required to receive the developing resistance and generate an additional effort to overcome it; it is the time of the reflex sensorimotor reaction implemented by proprioceptors of respiratory muscles [12].

The time parameters of these reflexes were studied during respiration without external resistance and with nonelastic resistance, in the capacity of which we used a set of tubes with a cone-shaped cross section, 2 to 16 mm in diameter, which were placed in the respiratory circuit in series with the pneumatographic tube and pneumatic valve.

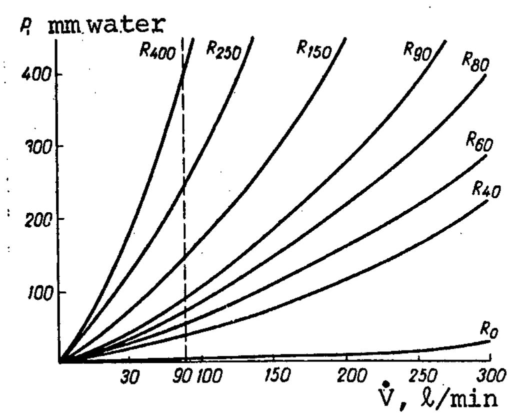

Figure 1.
Family of curves of tested nonelastic resistance (y-axis) as a function of volumetric velocity of constant flow of air (x-axis)
R_{40}-R_{400}) resistances (in mm water) with flow of 90 $\ell \cdot min^{-1}$

Figure 1 shows that the aerodynamic characteristics of the tested resistances were nonlinear. All of the resistances were arbitrarily referred to by the pressure required to maintain a constant flow of 90 $\ell \cdot min^{-1}$ through a given resistance. This flow is approximately equivalent to peak values on the pneumotachogram with a minute volume of about 30 $\ell \cdot min^{-1}$, i.e., with a moderate physical load, which was used in most of our studies.

The tests were conducted at rest and during performance of graded exercise on a bicycle ergometer. Exercise was performed in combination with R_0 resistance to respiration (control conditions without additional resistance) and with resistance in the range of 60-400 mm water (6.0-40.0 GPa) at $\dot{V}$ = 90 $\ell \cdot min^{-1}$ (R_{60}-R_{400}).

A Godart pneumotachograph was used to record the pneumotachogram and integrated spirogram; an Elema electric manometer was used to record pressure in the mouth (mouthpiece) or intrathoracic pressure measured in the lower third of the esophagus by means of a catheter with latex balloon containing 0.5 mℓ air.

Results and Discussion

It had been previously shown that relative hypoventilation (as compared to level in control conditions) and alveolar hypercapnia are the most typical respiratory reactions to nonelastic resistance to respiration [10, 11].

In a preceding investigation [3], it was established that a resistance of R_{60} does not elicit adverse subjective sensations either at rest or during

exercise, even with a maximum load, while the dynamics of tested objective physiological parameters showed virtually no difference with resistance R_0 and R_{60}.

Resistance R_{80} elicits sensory respiratory discomfort; however, we failed to demonstrate appreciable differences in objective parameters, as compared to control conditions, up to a heavy load on the order of 200 W. Upon further increase in the load, respiration becomes appreciably more labored. Concurrently, the increment of pulmonary ventilation starts to fall behind, while the increase in CO_2 content at the end of expiration starts to exceed the corresponding control levels.

With R_{250} labored breathing and dyspnea, relative hypoventilation and alveolar hypercapnia already appear with a load of 65-100 W, although the subjects are able to perform exercise up to 200 W.

With R_{400}, work capacity diminished drastically. Already with a load of 100-150 W, the subjects experienced severe dyspnea, which changed to asphyxia, and they stopped pedaling. Minute volume constituted about 60% of the control level, there was drastic increase in oxygen debt and anaerobic metabolism: blood lactases increased by 1.1-2.2 mmol/ℓ, as compared to the control load ($P<0.05$) [3].

When analyzing the results of this investigation, special attention should be given to the observed inconsistency between severity of subjective and objective components of physiological reactions to increasing resistance: already minor resistance to respiration (R_{80}) during exercise was associated with distinct respiratory discomfort, while greater resistance (R_{250} and R_{400}) elicited a feeling of markedly labored breathing, dyspnea, even asphyxia, and limited drastically physical work capacity. At the same time, the objective physiological correlates of these severe subjective sensations consisted mainly of insignificant changes in different directions in minute volume at rest and relative hypoventilation with a tendency toward hypercapnia during exercise.

The marked discrepancy between sensory and somatic reactions to resistance to respiration is apparently attributable to the presence of a rather powerful system for compensating the physiological changes, which provides adequate correction of cardiorespiratory parameters in the presence of functionally neutral, but sensorily significant resistance.

In view of the fact that compensatory reactions to resistance to respiration occur within microintervals of time, apparently the neuroreflex system of regulation plays the leading role in organizing these reactions [2, 12].

In order to examine the possible functional deficiency of this system, we studied the time characteristics of proprioceptive reflexes when breathing with resistance R_0, R_{150} and R_{250} during performance of three 15-min cycles of exercise of 100-150 W each at 15-min intervals between cycles (Figures 2 and 3). When breathing with resistance R_0, reflex time was 0.18 ± 0.015 s, and it did not change appreciably during all three exercise cycles. When breathing with R_{150} and particularly R_{250}, reflex time increased from cycle

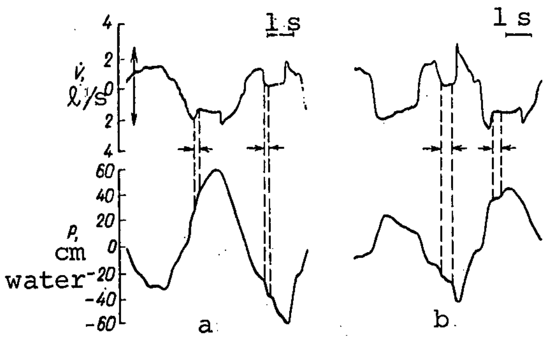

Figure 2.
Changes in duration of proprioceptive reflexes of respiratory muscles during breathing with external resistance and performance of exercise; arrowheads show duration of proprioceptive reflexes in inspiration (pointing up) and expiration (pointing down)

a) pneumotachogram and pressure in mouthpiece when air flow is interrupted during exercise of 150 W and breathing with resistance R_{250} in 15th min of 1st cycle of exercise
b) same in 15th min of 3d cycle of exercise

to cycle, reaching 0.29±0.012 and 0.38±0.06 s, respectively, by the end of the 3d cycle, i.e., it increased by more than double ($P<0.01$).

Apparently, the observed extension of sensorimotor reaction time of respiratory muscles should be interpreted as fatigue of respiratory muscles, which leads to functional deficiency of the proprioceptive system of regulating respiration.

It is known that the main purpose of regulating respiration is to provide for a minute volume that is consistent with the metabolic level and required to maintain gas homeostasis, while the controlled parameters are respiratory volume and rate [6]. The main functional indicator of change in lung volume is the length of intercostal muscles, in which the length of intrafusal receptors--sensors of length of muscles through supraspinal structures of the respiratory center and gamma loop--adjust themselves to the required respiratory volume, i.e., desirable muscle length, and generate impulsation of required force and frequency. As a result of α-γ coordination, thre is adequate contraction of extrafusal muscle fibers, thanks to which a specific respiratory volume is produced. Impulsation from intrafusal spindles attenuates to the point of disappearance in the event that the specified respiratory volume is reached.

If resistance to respiration appears, which does not permit realization of the specified muscle length with a normal exertion, the spindles remain extended and continue to send corrective impulses via alpha fibers, which cause motor neurons to become more active. Impulsation stops as soon as the length of extrafusal and intrafusal fibers is functionally equal and the specified respiratory volume is reached [2, 4, 9].

However, if the specified respiratory volume is not produced for some reason or other, a sensory discrepancy arises between what is "desired" and what is "achieved," which constitutes the basis of experiencing dyspnea [9].

This discrepancy is apparently the cause of the observed inconsistency between severity of subjective and objective reactions to resistance to respiration, and it is manifested by earlier onset of the sensory component of these reactions in relation to the autonomic one.

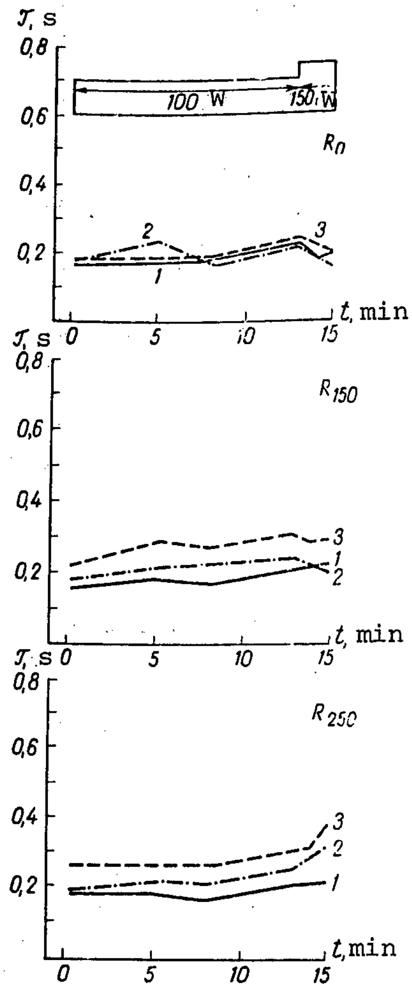

Figure 3.
Dynamics of duration of proprioceptive reflexes (τ) during 3 cycles of 100-150 W exercise when breathing without additional resistance (R_0) and with resistance R_{150} and R_{250}

Mean data for group are given, n=8

1-3) 1st-3d cycles, respectively

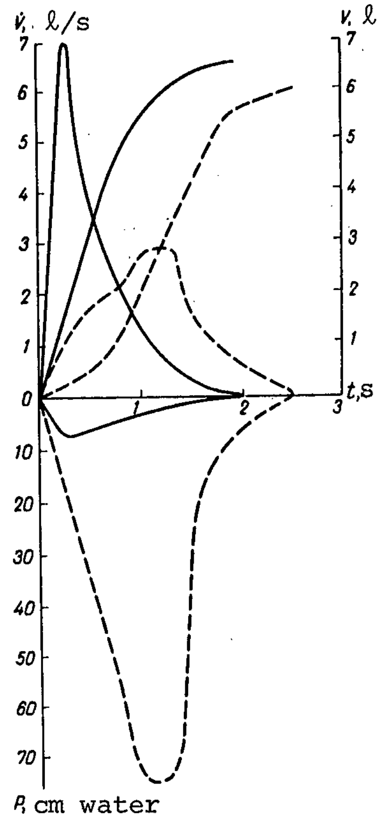

Figure 4.
Pressure-flow-volume function during forced expiration

Solid lines--expiration without resistance, dash lines--same with resistance R_{250}

Fatigue of respiratory muscles with resistance to respiration during exercise aggravates the sensory-autonomic dissonance, as a result of which sensations of labored breathing, dyspnea or asphyxia become the prime signs for determination of the limit of external resistance to respiration.

The second factor (other than the regulatory one) that limits this resistance is apparently referable to velocity and force characteristics of respiratory muscles.

When breathing with resistance, particularly when it is nonelastic, which alters its characteristics as a function of flow velocity, the respiratory muscles must constantly adjust their exertion to the resistance that changes

constantly during the respiratory cycle. In order to retain the usual dynamic stereotype of the respiratory cycle for velocity and volume parameters, correction of muscular exertion must be very flexible and take place within microsegments of time, i.e., it must be rapid. However, we know that the rate of contraction of skeletal muscles, specifically respiratory ones, is inversely proportionate to their load [7, 13].

This function was tested with forced expiration with and without external resistance. As an example, Figure 4 illustrates the pressure-flow-volume function, which indicates that during forced expiration with resistance R_0 maximum intrathoracic pressure in this subject, who is a trained athlete, constituted about 8 cm water, and this pressure provided for a maximum peak of air flow of 7 $\ell \cdot s^{-1}$ and expiration volume of 6.5 ℓ in 2 s.

During forced expiration with resistance R_{250}, intrathoracic pressure, which reflects exertion of expiratory muscles, increased almost 10-fold (about 80 cm water), but in spite of this the maximum velocity of flow of expiration decreased to less than half, to 2.8 $\ell \cdot s^{-1}$, the expiratory volume decreased insignificantly (to 6.0 ℓ) while expiration time extended to 2.5 s.

The group ($n = 6$) differences in the tested parameters of forced expiration with R_0 and R_{250} constituted ($M \pm m$) the following: intrathoracic pressure 3.8±0.19 and 44.2±0.36 cm water ($P<0.05$); peak velocity of expiratory flow 5.5±0.03 and 2.5±0.08 $\ell \cdot s^{-1}$ ($P<0.05$); expiratory volume 5.4±0.16 and 5.1±0.18 ℓ ($P<0.05$); expiration time 1.6±0.02 and 2.1±0.05 s ($P<0.05$), respectively.

Hence, it can be concluded that, with such resistance, respiratory muscles are capable of generating the required expiratory volume, but do not have time to accomplish this within the required time, since expiration occurs at a slower rate. The decrease in expiratory rate is apparently due predominantly to external resistance, rather than intensification of expiratory collapse, whereas the points of equal pressure that separate segments of the respiratory tract, which are or are not subject to collapse [14], must shift in a proximal (flow) direction when there is an obstruction to expiration, in the direction of segments with well-developed cartilage as protection against collapse.

Consequently, the burden on muscles that is generated by external resistance to respiration diminishes their force characteristics. As a result, a situation arises that is particularly typical of conditions where exercise is combined with respiratory resistance, when respiratory muscles are compelled to work harder within a constantly limited time. Upon reaching a certain level of such limitation and a certain limit of velocity and force capacities of respiratory muscles, there is a breakdown in regulation of respiration and development of relative hyperventilation with its subjective and objective manifestations, which were described above.

In conclusion, we can expound the hypothesis that, due to the speed of regulatory processes, which is ordinarily adequately implemented by the fusimotor proprioceptive system of respiratory muscles, voluntary regulation of respiration when there is additional external resistance could play some role at rest, but because of its static nature it must lose its relevance appreciably during exercise when time is acutely limited.

Thus, one should include functional deficiency of proprioceptive regulation of respiration and velocity-force qualities of respiratory muscles among the main factors that limit man's resistance to exogenous, nonelastic resistance to respiration.

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EFFECT OF HEMADSORPTION ON RHEOLOGICAL PARAMETERS OF BLOOD DURING SEVEN-DAY ANTIORTHOSTATIC HYPOKINESIA AND IN VITRO STUDIES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, May-Jun 86 (manuscript received 29 Jan 85) pp 50-53

[Article by I. B. Goncharov, A. P. Ivanov, A. F. Davydkin and Zh. M. Kudryashova]

[English abstract from text] The effect of hemosorption of blood rheology was examined in 9 healthy men exposed to head-down tilt (-8°). Venous-venous hemosorption was performed on tilt day 7 using activated charcoal SKN-2M. It was found that by tilt day 7 rheological parameters increased significantly and returned to the norm after 2-hour hemoperfusion through activated charcoal. This shows that hemosorption produces a beneficial effect on blood rheology and microcirculation which is indicated by a direct examination of eye microvessels. Experimental in vitro studies using oxygenated and nonoxygenated donor's blood demonstrated that hemosorption combined with blood oxygenation can noticeably increase the effectiveness of perfusion on the whole.

[Text] The investigations of several authors revealed that some rather substantial disturbances referable to rheological properties of blood are observed when motor activity is limited in animals [8, 9] and essentially healthy people submitted to hypokinesia in antiorthostatic position [head-down tilt] (HDT) and immersion [4]. Since HDT and immersion simulate some of the effects of weightlessness, one can also expect such disturbances of rheological parameters of blood in cosmonauts during flights and at the early stages of the recovery period. It is known that disturbances referable to rheological properties of blood and increase in its viscosity are present with many diseases of man. The severity of such diseases is apparently directly related to viscosity of blood [1-3, 5, 6, 10-13].

Proceeding from the foregoing, it is logical to believe that the changes in hemorheological parameters associated with most pathological states, and changes in these parameters under the influence of spaceflight factors could aggravate any disease and increase the risk of complications. Thus, normalization of rheological parameters of blood is felt to be one of the most important measures in comprehensive therapy when rendering emergency medical aid to cosmonauts.

Control of intoxication is another important measure in therapy when emergency states develop in cosmonauts, since the efficacy of traditional therapy and, consequently, outcome of the disease often depend on severity of toxicosis. In this respect, the most acceptable method of detoxification in space medicine is hemadsorption (HA). With HA, there is considerably faster improvement of patients' general condition, drastic reduction of signs of intoxication and in duration of intensive care [7].

Our objective here was to test the effect of HA on a number of rheological parameters of blood of individuals submitted to HDT (-8°) and in in vitro studies using normal and oxygenated donor blood.

Methods

Blood for hemorheological and hematological tests was drawn from subjects submitted to HDT from the cubital vein in the baseline period, 7 days before and on the 7th day after HA [sic]. We assessed hemorheology on the basis of parameters of apparent and caisson (C) viscosity of blood, coefficient of erythrocyte aggregation (A), range of viscosity of blood (τ_0), hematocrit (Hct) and concentration of hemoglobin (Hb). In addition, we measured intraocular pressure, pressure in the central retinal artery, caliber of arteries and veins of the retina. Rheological parameters of blood were determined using a rotation viscosimeter of the system of V. N. Zakharchenko at a temperature of 25±0.1°C. Viscosity of blood was measured at three shear rates: 0.5, 1.0 and 5.0 s^{-1}. Hb was measured by the cyanmethemoglobin method on an FEK-56M photoelectric colorimeter and Hct, on a hematocrit centrifuge by the conventional method.

Method of HA during HDT: HA was performed on the 7th day of HDT (-8°) on 9 essentially healthy men. SKN-2M activated charcoal was used as sorbent. Blood was perfused vein to vein (subclavian--cubital veins) through an adsorption column 400 cm^3 in size at the rate of 80-100 mℓ/min in 120 min.

Method of in vitro tests: blood (30 mℓ) was perfused in a closed system through SKN-2M hemadsorbent (adsorption column capacity 5 cm^3) for 20 min at a volumetric perfusion rate of 20 mℓ/min. Blood was oxygenated by means of direct contact of blood with oxygen for 10 min, and the pO_2 parameter increased by a mean of 100% after oxygenation, as compared to the base level.

Results and Discussion

Table 1 lists the results of hemorheological studies under HDT conditions.

The data listed in Table 1 indicate that there were substantial changes in most tested rheological parameters of blood. For example, on the 7th day of HDT, apparent viscosity of blood at shear rates of 0.5, 1.0 and 5.0 s^{-1} was reliably greater ($P<0.01$) than the initial level by 55.1, 55.6 and 69.3%, respectively. Maximum changes on the 7th day of HDT were observed in caisson viscosity which increased by a mean of 87.2% ($P<0.01$).

After HA, the rheological parameters of blood showed virtually no difference from the baseline. It is important to mention that the indicator of range of

blood viscosity was lower (P<0.05) after HA than before hemoperfusion by a mean of 40.4%.

Table 1. Mean hemorheological parameters before and after hemadsorption in subjects submitted to HDT (M±m)

Period	Apparent viscos., cp shear rate, s^{-1}			C, cp	τ_0, dyne/cm^2	A, dyne/$cm^2 \cdot 10^{-6}$	Hb, g/ℓ	Hct, %
	0,5	1,0	5,0					
Baseline	22,7±1,8	16,2±1,3	8,8±0,7	4,7±0,5	0,0357±0,0044	0,591±0,060	166,3±3,5	46,1±0,8
Before HA, 7th day	35,3±2,0*	25,2±1,5*	14,9±1,0*	8,8±0,6*	0,0438±0,0044	0,519±0,150	186,9±3,3*	50,4±0,7*
After HA, 7th day	22,0±1,2	16,1±0,8	9,0±0,5	4,8±0,4	0,0312±0,0026	0,582±0,060	164,2±2,2	46,4±1,3

*P<0.01, as compared to baseline.

The changes in concentration of hemoglobin and hematocrit coincided with those referable to viscosity (see Table 1).

Thus, the investigations revealed significant rise of rheological parameters of blood and hematological parameters by the 7th day of HDT, which reverted to the baseline after 2-h hemoperfusion through activated charcoal. This is indicative of the beneficial effect of HA on hemorheological parameters and, consequently, on the microcirculatory system, as indicated by direct examination of microvessels of the eye in the baseline period, on the 40th and 60th min of HA (Table 2).

Table 2. Microcirculatory parameters before and during HA on 7th day of HDT (M±m)

Parameter	Before HA	HA 40 min	HA 60 min
Pressure in central retinal artery, mm Hg	45,3±0,8	44,9±2,1	46,1±0,7
Retinal artery caliber, µm	77,4±3,1	83,9±4,7*	97,2±3,4**
Retinal vein caliber, µm	143,3±3,6	175,6±4,2**	175,0±3,6**
Intraocular pressure, mm Hg	17,1±0,4	16,2±0,4	15,9±0,2**

*P<0,05.
**P<0,01.

On the basis of these data, it can be concluded that HA had no appreciable effect on pressure in the central retinal artery. At the same time, intraocular pressure dropped reliably (P<0.01) by a mean of 7.5%. In addition, after HA there was also decline of tonus of retinal vessels. These facts are indicative of improvement of blood flow in the microcirculatory system, which is apparently related to normalization of hemorheology. However, we did not obtain a reliable answer as to the direct effect of HA on hemorheological parameters and microcirculation in this series of investigations, since up to 500 mℓ fluid (saline) was given to all subjects in the course of perfusion.

In vitro tests with donor blood precluded administration of any solutions during perfusion, which permitted evaluation of the direct effect of HA on hemorheological parameters (Table 3).

Table 3. Hemorheological and hematological parameters of donor blood before and after HA (M±m)

Period	Appar. viscosity, cp shear rate, s^{-1}			C, cp	τ_0, dyne/cm^2	A, dyne/$cm^2 \cdot 10^{-6}$	HB, g/ℓ	Hct, %
	0,5	1,0	5,0					
Before HA	18,5±2,0	14,2±1,4	8,9±1,0	5,8±0,8	0,020±0,004	0,703±0,13	128,4±5,0	40,8±1,0
After HA	14,0±1,2	10,5±0,9*	6,6±0,6	3,9±0,4*	0,015±0,002	0,448±0,040**	128,2±4,5	38,5±1,0

* $P < 0,05$.
** $P < 0,01$.

Table 4. Hemorheological and hematological parameters of oxygenated donor blood before and after HA (M±m)

Period	Apparent viscosity, cp shear rate, s^{-1}			C, cp	τ_0, dyne/cm^2	A, dyne/$cm^2 \cdot 10^{-6}$	Hb, g/ℓ	Hct, %
	0,5	1,0	5,0					
Baseline	18,5±2,0	14,2±1,4	8,9±1,0	5,8±0,8	0,020±0,004	0,703±0,13	128,4±5,0	40,8±1,0
After oxygenation	13,9±1,7*	10,0±1,0	5,8±0,6	3,4±0,5	0,020±0,005	0,487±0,08	110,1±19,3	39,5±1,2
After HA	12,1±1,3*	9,3±1,0*	5,9±0,8	3,9±0,6*	0,010±0,002	0,415±0,04*	127.2±3,36	38,0±0,9

*P<0.05, as compared to baseline.

The results listed in Table 3 are indicative of reliable decline of most tested rheological parameters (including viscosity of blood) after hemoperfusion. At the same time, Hb and hematocrit showed virtually no difference from baseline values. It is important to note that toxicity of blood, according to the Paramecium test, decreased (P<0.01) by a mean of 58%. Thus, the findings are indicative of beneficial effect of HA on rheology and toxicity of blood.

It is known that severe intoxication associated with human diseases is accompanied by respiratory insufficiency to some extent or other, whereas hemadsorbents actively absorb oxygen from blood. In this regard, we tested the effect of HA on rheological parameters of oxygenated donor blood (Table 4).

The results indicate that direct oxygenation of blood had an appreciable effect on most tested rheological parameters of blood. Thus, apparent blood viscosity decreased reliably by a mean of 41.4% at a shear rate of 1.0 s^{-1} and by 52.4% at a shear rate of 5.0 s^{-1}. Maximum change was referable to caisson blood viscosity, which dropped by a mean of 70.4% after oxygenation.

The rheological parameters of oxygenated blood after HA appear to be preferable to analogous results of HA for nonoxygenated blood. It is important to note

that toxicity of blood according to the Paramecium test decreased by a mean of 68.5% with the combination of HA and blood oxygenation after perfusion, as compared to the baseline.

These investigations revealed that HA, which is a powerful means of detoxification, also improves significantly the rheological parameters of blood. This is particularly important if we consider that one can expect an increase in viscosity of blood during spaceflights, even in healthy people. In addition, HA has a beneficial effect on the microcirculatory system, and combining it with oxygenation enhances appreciably the efficacy of perfusion as a whole.

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EFFECT OF LONG-TERM SPACEFLIGHT ON RAT BRAIN POLYAMINE CONTENT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
Vol 20, No 3, May-Jun 86 (manuscript received 13 Jun 85) pp 53-57

[Article by R. A. Tigranyan and V. Yu. Kovalev]

[English abstract from source] The concentration of polyamines, i.e. putrescine, spermidine and spermine, was measured in different brain compartments of rats flown for 18.5 days on Cosmos-1129. Exposure to space flight led to changes in the polyamine content that were the most distinct in medulla oblongata. It is suggested that the changes develop as a result of a chronic stress associated with the effects of weightlessness.

[Text] During long-term flights aboard biosatellites of the Cosmos series, changes were demonstrated in the rat central nervous system that were attributed to the effect of weightlessness and various stress factors [1-4]. Our objective here was to investigate the levels of polyamines (putrescine, spermine and spermidine) in different parts of the rat brain after a spaceflight aboard Cosmos-1129 biosatellite. Polyamines are considered to be indicators of intensity of protein biosynthesis [10], since they stimulate it on the level of DNA transcription [9, 11]. Such studies had not been conducted previously.

Methods

The investigations were conducted on male Wistar-SPF rats (Bratislava, CSSR) flown for 18.5 days in space aboard Cosmos-1129 biosatellite. The animals were submitted to euthanasia 6-8 h and on the 6th day after completion of the flight. Some of the animals examined on the 6th postflight day were submitted to immobilization stress 5 times (150 min daily). The control and synchronous groups of rats were also submitted to repeated immobilization. There were 6-7 animals in each experimental and control group. The concentration of polyamines in parts of the brain selected according to a special scheme [5] (hemispheres, cerebellum, medulla oblongata, hypothalamic region) was determined by ion-exchange chromatography followed by electrophoresis in supernatants recovered by centrifuging homogenates of tested parts of the brain at 11,000 r/min for 15 min at a temperature of +4°C [6]. The obtained data were calculated per unit protein [8]. Statistical reliability was determined using Student's t-test.

Results and Discussion

Immediately after the experiment, there was significant increase in putrescine, spermine and spermidine content of the medulla oblongata in flight and synchronous experiment groups of animals, as compared to the vivarium control. In the cerebellum, putrescine and spermine concentrations were considerably lower in flight and synchronous groups than in the vivarium control. Spermidine level rose in both the flight group and synchronous experiment, as compared to control values. In the hypothalamic region, there was increase in concentrations of putrescine, spermidine and spermine immediately after the flight, in rats of the synchronous and, particularly, flight groups, as compared to the vivarium control. The cerebral hemispheres of flight and synchronous groups of animals failed to reveal reliable changes in polyamine levels, as compared to control values; however, putrescine, spermidine and spermine levels were higher in flight animals than in rats used in the synchronous experiment (Figure 1).

Six days after the experiment, spermidine concentration in the medulla oblongata of flight and synchronous groups of rats still exceeded significantly the levels for the vivarium control. Spermine content in flight animals exceeded appreciably the values for both control groups of rats. Putrescine content in the flight group of rats was one-half the level in animals of the vivarium control, although this parameter was 2.5 times higher in the synchronous experiment than in the control. In the same period, there was a decrease in cerebellar concentration of putrescine in animals of the synchronous experiment and in spermine of rats in the flight and synchronous groups, whereas spermidine content increased in flight animals. In the hypothalamic region, the concentrations of putrescine and spermidine 6 days after termination of the experiment decreased significantly, as compared to the vivarium control. We found an increase in putrescine and spermine concentration in flight animals (as compared to vivarium control). At this time, the cerebral hemispheres of rats in the synchronous experiment failed to reveal changes in polyamine concentration. Putrescine and spermidine content was significantly higher in the flight group of animals than in the vivarium control (Figure 2).

Repeated use of immobilization stress in the postexperimental period led to increase in spermine concentration and decrease in putrescine content in the medulla of rats used in the synchronous experiment. Flight animals presented significant elevation of putrescine level with concurrent drop in spermidine. Cerebellar levels of spermidine rose, while concentrations of putrescine and spermine decreased in the cerebellum of animals in the synchronous experiment. The flight group of rats presented significant decline of putrescine, spermidine and particularly spermine levels. In the hypothalamic region, flight animals showed an increase in all polyamines, whereas rats of the synchronous experiment presented a decrease in concentrations of putrescine, spermidine and spermine. Repeated immobilization stress in the recovery period was associated with decrease in spermidine content of the cerebral hemispheres in animals of the flight and synchronous experiment groups (Figure 3).

The results of these investigations indicate that maximum changes in polyamine levels of flight animals were observed in the medulla oblongata, the greatest change being referable to putrescine concentration and the least, to spermine.

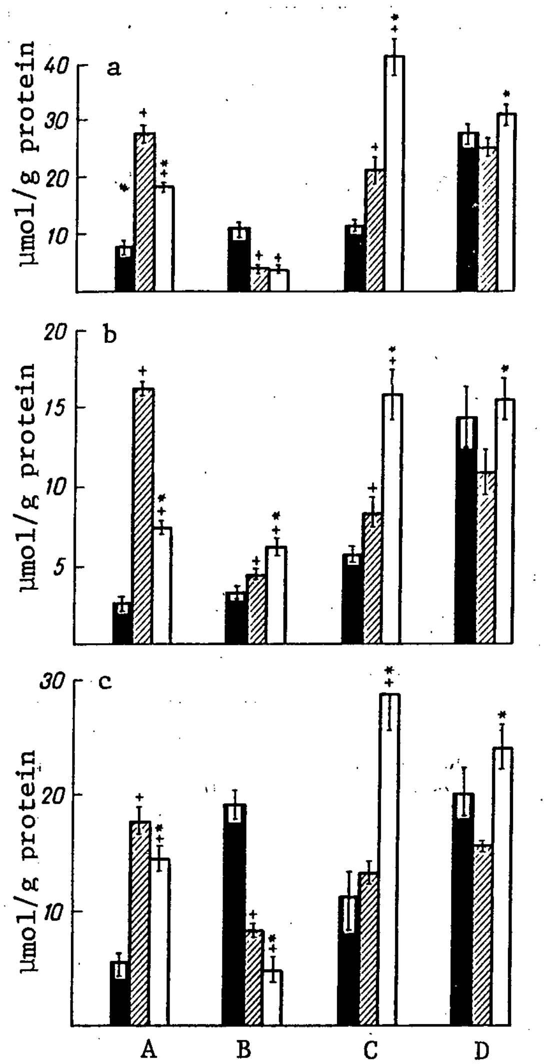

Figure 1.
Polyamine content of different parts of the rat brain immediately after flight aboard Cosmos-1129
Here and in Figures 2 and 3:
a) putrescine
b) spermidine
c) spermine
A) medulla oblongata
B) cerebellum
C) hypothalamic region
D) cerebral hemispheres
Black bars--control, striped--synchronous control, white--flight
+) reliable differences from control
*) reliable differences between flight and synchronous groups

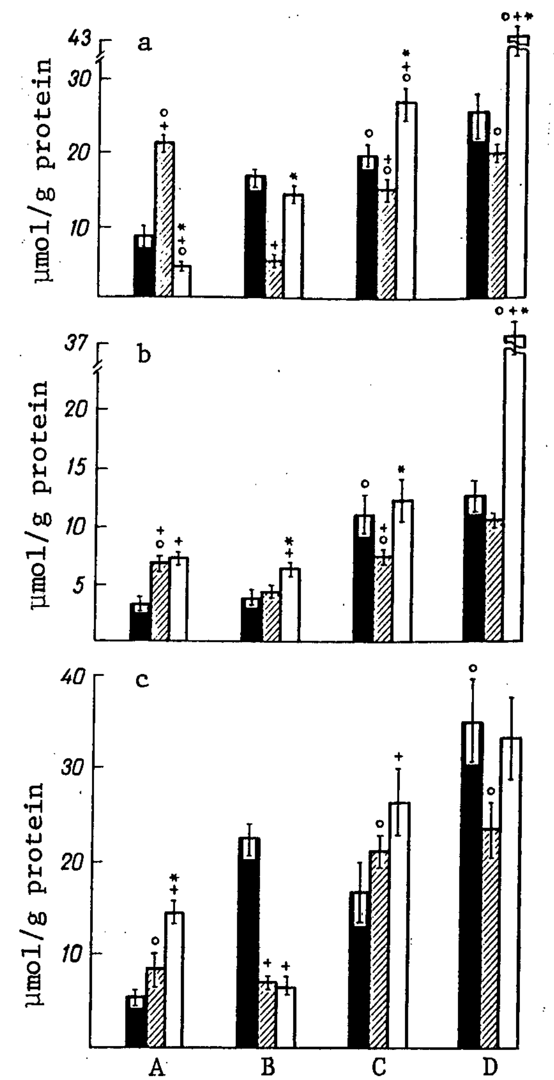

Figure 2.
Polyamine content of different parts of the rat brain 6 days after flight aboard Cosmos-1129 biosatellite
Here and in Figure 3, circles show differences from parameters obtained immediately after the experiment

Immediately after the experiment, the flight and synchronous groups of animals presented similar changes; however, the concentrations of polyamines changed in different directions in different parts of the brain. This is most probably related to differences in intensity of adaptation processes in different parts of the brain. No significant changes in

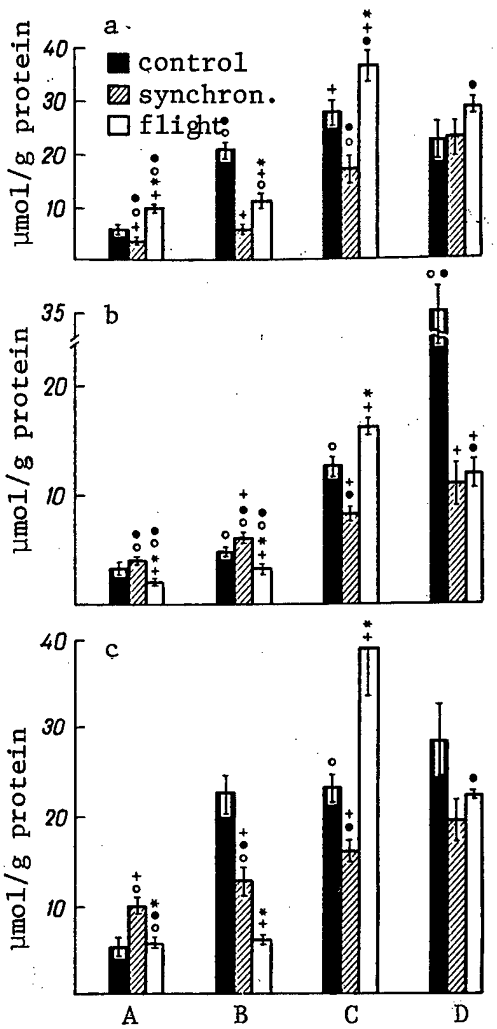

Figure 3.
Polyamine content of different parts of the brain of rats submitted to repeated immobilization after landing, 6 days after completion of flight aboard Cosmos-1129
The dots refer to differences between parameters obtained on the 6th postexperimental day and animals submitted to repeated immobilization in this time

polyamine content were demonstrable in the cerebral hemispheres of rats in the flight and synchronous groups. This suggests that extreme factors related to spaceflight initiated adaptive reactions, thanks to which there was normalization of polyamine concentration in this part of the brain. In addition, the assumption that there was overexcitation in the cerebral hemispheres during spaceflight, as a result of which they could no longer react to extreme factors related to landing of the biosatellite, is quite plausible.

Immediate postflight concentration of spermine was elevated in all tested parts of the brain, with the exception of the cerebellum. The decrease in cerebellar spermine content in the presence of significant increase in concentration of spermidine (see Figure 1), from which spermine is synthesized, can be attributed to attenuation of the effect of the enzyme, spermine synthetase, which is responsible for spermine synthesis. The marked increase in spermine content in other parts of the rat brain after the spaceflight suggests that there is also another mechanism involved in its synthesis, which is unrelated to attachment of the amino propyl group to the existing spermidine. Analogous data were obtained in a study of distribution of radioactive tracer in spermidine and spermine after administration of labeled putrescine [8].

Readaptation to earth's gravity for 6 days led only to partial normalization of polyamine concentration in different parts of the brain. After 6 days of recovery, the flight group of animals revealed virtually the same levels of polyamines in the medulla, cerebellum and hypothalamic region as were found immediately after landing. This similarity of findings immediately after landing and on the 6th day of the recovery period could be attributed to the continuing effect of adaptive metabolic changes, which began during the flight. At the same time, the concentration of polyamines increased significantly in flight animal cerebral hemispheres 6 days after landing, as compared to the levels of these compounds immediately after the flight. Evidently, this indicates that 6-day recovery led to activation of processes of polyamine synthesis in the cerebral hemispheres.

It is interesting to note that, unlike the tests performed immediately after landing, the data obtained on the 6th day of recovery showed a marked difference in concentration of tested compounds in the brain of flight and synchronous groups of animals. The only exception was spermine, which changed in the same direction in both groups of rats. This discrepancy is most probably attributable to the effect of weightlessness, a factor that cannot be simulated for a long time on earth and, consequently, neither can it be reproduced in the synchronous experiment. The similarity of findings for flight and synchronous groups immediately after the experiment can apparently be also attributed to the fact that the changes in polyamine content were leveled off in the presence of emotional stress in the rats, which was related to landing of the biosatellite.

We used a test involving repeated immobilization stress [7] in order to determine the nature of the stress reaction in animals that had been flowin in space for a long time and to answer the question of whether spaceflight is an acute or chronic stressor. The tests revealed that different parts of the brain of flight animals reacted differently to immobilization stress. Analysis of the obtained data enables us to conclude that spaceflight factors affected the central nervous system of flight rats like a chronic stressor impulse. However, the nerve centers of the hypothalamus and medulla oblongata were apparently able to adapt faster to stress conditions. Chronic stress related to weightlessness most probably elicited a change in cerebellar and hemispheric nerve centers, and this affected the stability and tolerance of protein-synthesizing mechanisms.

On this basis, we can interpret postflight changes in polyamine content as the result of a prolonged, stepped adaptive reaction that develops during constant exposure to spaceflight factors.

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EFFECT OF HYPOXIA ON DNA SYNTHESIS AND COLLAGENT CONTENT OF REGENERATING SKIN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
Vol 20, No 3, May-Jun 86 (manuscript received 20 Dec 84) pp 57-61

[Article by G. V. Khomullo, V. I. Lotova, A. N. Chernyayev and I. N. Vinogradov]

[English abstract from source] During chronic hypoxia DNA synthesis in various areas of the regenerating skin decreased. Inhibition of epithelial and connective-tissue elements was accompanied by suppression of collagenogenesis, which finally led to longer-term wound healing.

[Text] Delayed posttraumatic regeneration of the skin in the presence of chronic hypoxia had been noted in experiments on animals, in which hypoxia was produced by means of prolonged inhalation of hypoxic gas mixtures [14, 16, 17], as well as in studies of wound healing at high altitude, where low atmospheric pressure and related decrease in partial oxygen pressure are among the main factors that have an effect on the body [1, 4].

At the same time, it should be noted that the few investigations of the effect of chronic hypoxia on skin regeneration are usually limited to recording only the general morphological signs of healing, without analysis of cytological, ultrastructural, metabolic and other morphological and functional changes in regenerating structures.

Previous studies revealed that the cytological composition of wound exudate [5] and ultrastructure of granulation tissue fibroblasts in regenerating skin wounds are altered under hypoxic conditions [9]. Our objective here was to investigate the proliferative activity of different zones of regenerating skin and collagen content of granulation tissue at different stages of the repair process.

Methods

Experiments were performed on 80 male white rats. The animals were divided into 2 groups: control (production of full-layer wounds 225 m^2 in area) and experimental (wounds + chronic hypoxia throughout the healing period). Hypoxia was produced by the pressure chamber method: throughout the experiment, the

animals were kept in a pressure chamber for 8-10 h per day at a pressure of 250-260 mm Hg ("altitude" of 8500-8200 m above sea level). "Ascents" and "descents" were made at the rate of 25-30 mm Hg/min. DNA synthesis in different zones of regenerating skin was examined by autoradiography using ^{3}H-thymidine. The isotope was injected intraperitoneally in a dosage of 0.5 μCi/g weight 5 and 10 days after producing wounds, 3, 6 and 24 h before decapitation. We calculated the index of labeled nuclei (ILN) in five different zones, and expressed it as a percentage. Collagen was extracted from granulation tissue by the method of Fitch et al. as modified by L. I. Slutskiy and I. I. Shelekitina [8], and this was followed by assay using the colorimetric method described by Lowry et al. [15]. In addition, for objective evaluation of rate and nature of repair process, we measured the wound area, and various elements of the healing wound on histological preparations stained after Mallory, using an ocular micrometer.

Results and Discussion

Measurement of wound area revealed that the wound defect healing is slower under hypoxic conditions than in the control. Thus, wound area constituted 115±8.56 mm^2 5 days after sustaining trauma in control animals and 160±8.29 mm^2 in the experimental group ($P<0.05$); the figures after 10 days were 24±1.76 and 43±4.43 mm^2, respectively ($P<0.05$). Complete healing of the wound defect with formation of a cicatrix occured by the 13th day of observation in control rats, whereas in hypoxic rats healing ended on the 15th-17th day.

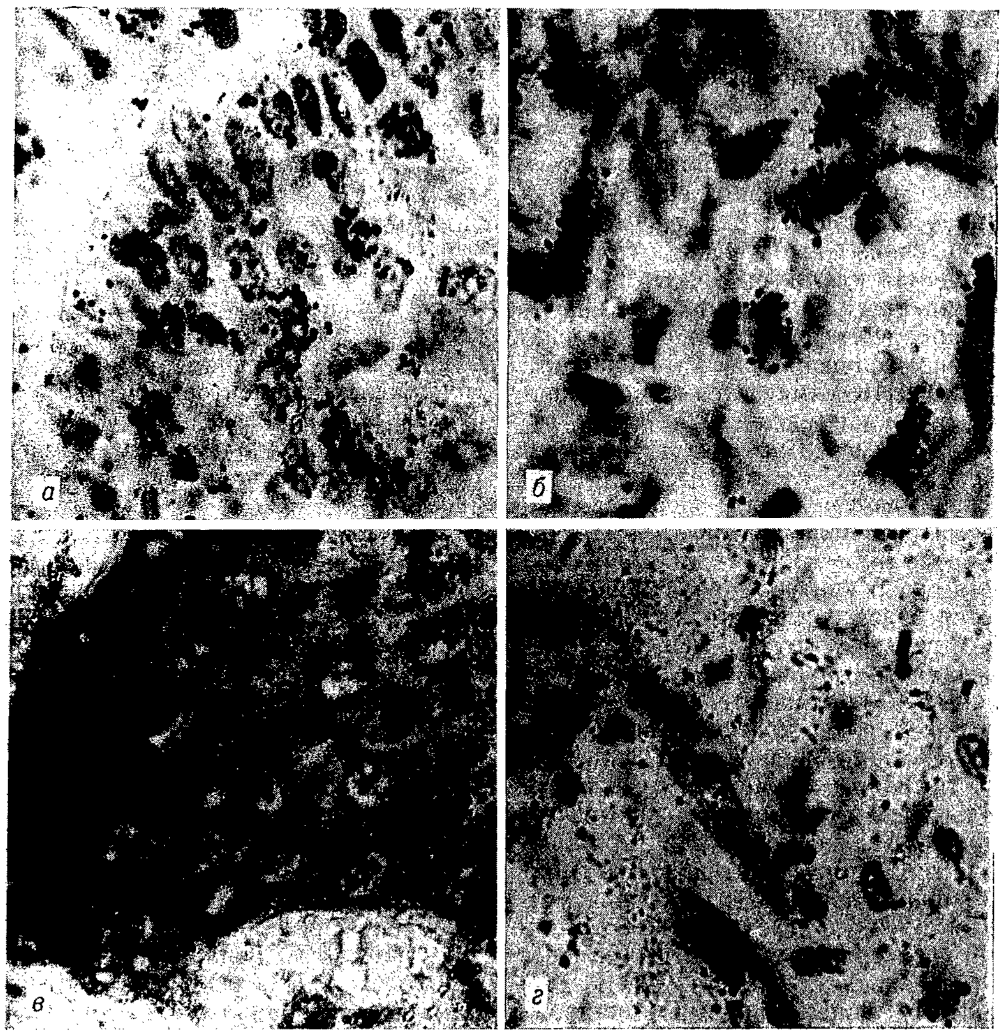
Examination of histological preparations revealed slow formation of granulation tissue, which was associated with progressive destructive and dystrophic changes in cellular elements, newly formed vessels and fibrous structures. Granulation tissue was formed in foci between fatty tissue cells, and it was characterized by a number of morphological changes: edema, destruction of cellular elements (most often in the form of pyknosis of nuclei) and disintegration of collagen fibers. There was development of marked dyscirculatory processes manifested by paretically dilated blood vessels with thinned down walls, signs of plasmorrhagia and presence of hemorrhages.

The slow development of granulation tissue in the presence of hypoxia delayed growth of new epithelium, which presented degenerative changes in the form of nuclear pyknosis and vacuolization of cytoplasm.

The morphological examination, which revealed a lag in reduction of thickness of scab and leukocytic ridge, increase in thickness of granulation tissue and regenerative epithelium, was entirely consistent with the above-described histological changes (Table 1).

Examination of proliferative activity of tissue in 5-day old regenerated skin of control animals revealed that maximum ILN was demonstrable 24 h after injection of the isotope (Table 2). A maximum number of epithelial cells that took up ^{3}H-thymidine was situated in the basal and spinous layers of the boundary zone of the epidermis (see Figure, *a*). Isolated cellular elements synthesizing DNA were demonstrated in the epithelial regenerate. There were none in the region of the free edge of the epithelial layer, and their number increased gradually toward the epidermal boundary zone. Intact

epidermis surrounding the wound participated actively in regenerative processes. In sections of this epidermis 1-1.5 mm away from the edge of the wound there was a significant number of labeled cells. ILN was somewhat higher at this time in young connective tissue covered by regenerated epithelium than in granulation tissue, and in new connective tissue ^{3}H-thymidine was incorporated mainly by fibroblasts and endothelial cells, whereas in granulation tissue adventitial cells were also often labeled, and polyblasts less often; this applied also to lymphocytes in the top granulation layers (see Figure, *б*).



Incorporation of ^{3}H-thymidine in cell nuclei of epithelial border zone (*а*, *в*) and granulation tissue (*б*, *г*), 5 days after surgery (24 h after injection of isotope); hematoxylin stain, magnification 1200×
а, *б*) control
в *г*) experimental animals

Table 1. Thickness of different elements of healing wound under hypoxic conditions (in μm)

Duration of hypoxia	Animal group	Leukocyte ridge	Granulation tissue	Epithelium	
				on margin of defect	regenerate
5 days	Control	70±4,6	455±14,4	235±13,3	104±9,0
	Experiment	141±7,4	350±14,8	158±10,2	45±2,2
10 days	Control	37±3,3	1346±79,0	207±13,1	128±24,9
	Experiment	86±3,3	680±97,0	151±12,7	70±4,2

Note: Here and in Table 3, $P<0.05$ in all cases as compared to parameters for control group

Table 2. ILN in epithelial and connective tissue cells (%; 24 h after ^{3}H-thym.)

Animal group	Epithelial wedge	Epithelial border zone	Intact epidermis	Young connective tissue	Granulation tissue
5 days after surgery					
Control	5,9±0,38	24,5±1,28	14,2±0,47	26,2±0,82	18,0±0,51
Experiment	4,8±0,44	13,0±0,83*	8,8±0,65*	—	12,1±0,75*
10 days after surgery					
Control	6,2±0,58	24,2±1,01	14,4±1,04	15,7±0,87	16,5±0,34
Experiment	5,3±0,63	17,6±0,89*	10,8±0,51*	12,8±0,49*	13,3±0,47

In the presence of chronic hypoxia, cell capacity to incorporate ^{3}H-thymidine was diminished in all zones of the regenerate. Hypoxia had a maximum depressing effect on DNA synthesis in the epidermal boundary zone (see Figure, *в*), where the number of labeled cells was almost 1/2 the number in the control. Mitoses were seldom encountered. The first labeled mitoses appeared only 6 h after injection of ^{3}H-thymidine, whereas in the control they were demonstrable after 3 h. Unlabeled mitoses were not encountered after 24 h. Proliferative activity of connective tissue cells was considerably lower than in the control at this time; among cells in granulation tissue that had take up thymidine there was prevalence of adventitial cells situated along the blood vessels, polyblasts and lymphocytes (see Figure, *г*).

The patterns of distribution of tracer demonstrated after 5 days also persisted 10 days after surgery in control animals. ILN in the boundary zone of epidermis remained high, as before, due to continuing intense epithelization of the wound surface. Conversely, proliferation of connective tissue was diminished at this time due to its differentiation and maturation; the number of labeled cells in granulation tissue was insignificantly higher than in newly formed connective tissue.

In this period, the number of DNA-synthesizing cells in the boundary zone and intact epidermis of experimental animals increased somewhat, as compared to the preceding period, but remained considerably lower than in the control. The decrease in number of DNA-synthesizing cells in the region of the epithelial regenerate was unreliable. Such autonomy of the free end of the epithelial

wedge could be due to impairment of its circulation and innervation [3]. The number of labeled connective tissue cells increased 10 days after surgery, mainly at the expense of adventitial elements and endothelium, which is probably related to intensified development of vessels in the regenerated skin with inadequate delivery of oxygen.

The amount of collagen, as shown by the studies, increased consistently in granulation tissue of control rats by the 10th observation day, decreasing somewhat after 15 days (Table 3). Collagen content of granulation in rats submitted to chronic hypoxia reached a maximum only after 15 days, but was below the control level throughout the experiment ($P<0.05$).

Table 3. Collagen content of granulation tissue during healing of skin wounds (% dry tissue weight)

Group of animals	Observation time, days		
	5	10	15
Control	10.60±2.34	33.92±0.59	28.95±1.98
Experimental	6.65±1.09	11.97±3.24	23.05±1.28

Our findings lead us to conclude that chronic hypoxic hypoxia is a factor that drastically depresses repair regeneration of skin. Slower formation of granulation tissue, conditions for which are depression of inflammatory reaction, qualitative and quantitative impairment of cellular composition of wound secretions with a shortage of energy resources that we reported previously [5, 6], is largely due to inhibition of proliferative processes under hypoxic conditions. This could be related not only to inadequate energy supply for anabolic processes, but excessive migration into blood of glucocorticoids [2, 11], which extend all phases of the cell cycle and block passage of cells from the postmitotic phase to that of DNA synthesis [7, 10]. The drastic decrease in collagen content of granulation tissue at all stages of healing apparently occurs as a result of impaired kinetics of collagenogenesis. It is known that proline and lysine hydroxylation processes, which take place at one of the stages of biosynthesis of protocollagen [18], are aerobic and occur with the use of atmospheric oxygen [12, 13].

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ELECTRODERMAL CONDUCTIVITY IN MAN AND MONKEYS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 22 Feb 85) pp 61-68

[Article by A. T. Neborskiy and G. S. Belkaniya]

[English abstract from source] The topographic and functional correlation of acupuncture skin zones on the limbs of humans (99 healthy subjects) and monkeys (64 adult hamadryas baboons and rhesus-monkeys) was compared by measuring the electric conductivity of the skin (ECS). The profile of the ECS was found to be an informative and sensitive integrated indicator of the functional state of the body and of the autonomic nervous system. The parameter ECS showed seasonal variations and relief differences with respect to the two phases of the menstrual cycle in women. The parameter ECS displayed distinct differences between men and women as well as species differences between men, hamadryas baboons and rhesus-monkeys. The high differential informativeness of the ECS is indicated by the functional differences of the primate body under various constraint conditions. The anatomical and topographic correlation of acupuncture skin zones and similarity of ECS characteristics in man and monkeys suggest that the formation of functional characteristics of the ECS in various types of primates has a common philogenetic basis. It is concluded that monkeys can be used as an adequate experimental model for further evaluation of the ECS as a method to measure and diagnose functional and pathological changes in the body.

[Text] Biophysical methods are being used more and more at the present time to assess the functional state of the body, different physiological systems and organs. The desirability of using such methods is attributable to the relative simplicity and clinical nature of the methods, as well as possibility of obtaining objective and quantitative information. Among the contemporary diagnostic procedures based on measurement of biophysical parameters, measurement of electric conductivity of the skin is of definite interest.

This method is based on the conception of relationship between functional state of internal organs and electric characteristics of projection zones of the skin over the arc of the viscerocutaneous sympathetic reflex [5, 9, 11, 12].

The galvanic skin response (GSR) was previously described as the phenomenon of change in difference between skin potentials and decrease in skin resistance in the presence of emotional and mental stress [3, 6, 12]. Results of investigations revealed that GSR, or the Tarkhanov phenomenon, reflects general reactivity of the autonomic nervous system [8]. It should be noted that, traditionally, the GSR was tested apart from projection zones of the skin, and its use was found to be informative enough to assess general reactivity of the body when examining higher nervous activity under normal and pathological conditions, and determining the range of threshold sensibility of sense organs [2, 10]. In addition, the advantages and informativeness of polygraphic registration of GSR in Zakharyin-Head zones were demonstrated [7].

It can be assumed that a combination of measurement of electrical characteristics of the skin with the system of body meridians that is used empirically in contemporary reflex therapy, which is essentially a system of projection skin zones of interval organs, would enhance the informativeness of the diagnostic method based on measurement of electrodermal conductivity [13]. The existing experimental and clinical data indicate that functional or pathological changes in internal organs are reflected in electric conductivity of corresponding projection zones of the skin, and they can confirm either a state of health or disease of the body as a whole, as well as, perhaps, the functional or pathological state of its organs and physiological systems [1, 4].

In this respect, it is deemed important to develop the physiological basis for using the method of measuring electrodermal conduction (EC) in functionally reflected cutaneous visceral projection systems. In addition to clinical validation, it is of unquestionable importance to pursue experimental studies and modeling on animals of various functional and pathological states. Since the obtained data are extrapolated to man, the choice of experimental model acquires special significance. The principle of concrete morphological and functional correspondence must be followed here.

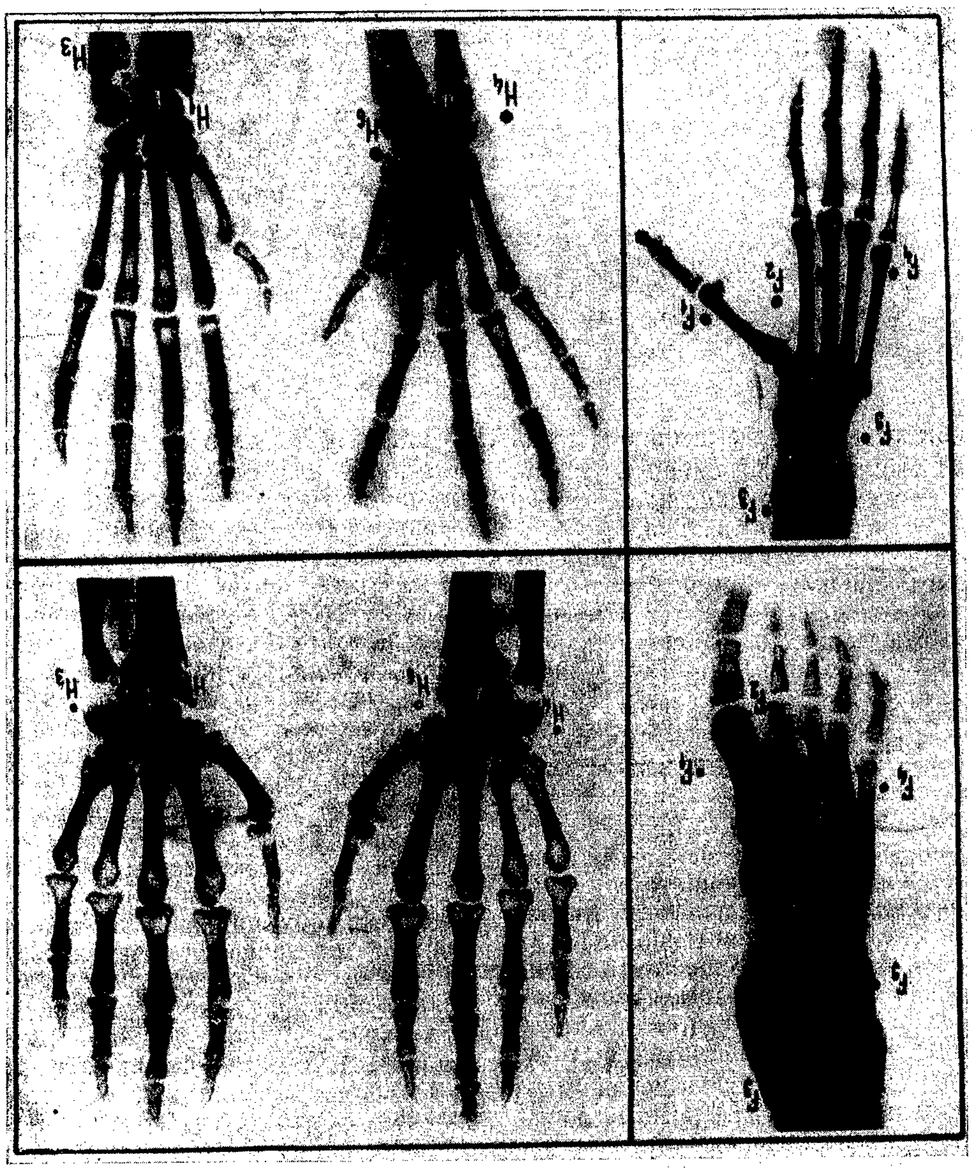
Our objective was to make a comparative analysis of topographic and functional correspondence of acupuncture zones on the limbs of man and monkeys.

Methods

The clinical studies were conducted on 46 healthy men and 53 women 18-40 years of age. Experimental studies were conducted on two species of monkeys that are used the most in biomedical research: adult hamadryas baboons and Macaca rhesus.

A standard method was used to measure EC. The measuring electrode, with a working area of 1 cm^2, saturated in saline, was applied to the tested skin zone. The silent electrode, in the form of a round convex plate, was attached with an elastic clamp to the surface of the palm; it too was soaked in saline. Measuring time, which was monitored with a special device, did not exceed 3 s. The measured EC was automatically fixed by the pointer of a microammeter. The recording device was turned off for each successive measurement. To measure EC we used a system of symmetrical acupuncture zones on the skin (AZS) of the limbs [9, 11, 12, 13]. This system consisted of 12 zones in the

region of the wrist (H_1-H_6, on the right and left) and 12 zones (F_1-F_6, on the right and left) in the region of the feet and ankle joints (Figure 1).



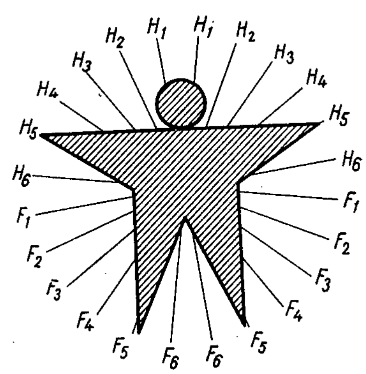


Figure 1.
Anatomical and topographic homogy of AZS on x-rays of human (top) and simian (bottom) foot and hand

On the right, drawing of AZS system of the limbs in polar coordinates; explained in the text

The measured EC (in μA) were plotted on the corresponding axes of a polar diagram. The EC profile (ECP) was constructed from EC measurements in 24 AZS.

We used mean EC for all 24 AZS ($\overline{EC}$), as well as EC separately for upper (EC_H) and lower (EC_F) extremities, left (EC_s) and right (EC_d) leads, as the general integral parameter. Uniformity of distribution of EC in all zones (ΔEC) was assessed from the difference between maximum and minimum ECP. We determined lateral (d/s) and transferse (H/F) asymmetry as the asymmetry indicator. As we know, the internal and external surfaces of the skin on the limbs are characterized by specific functional distinctions. For this reason, we took into consideration the ratio of internal AZS to external EC (i/e).

EC was measured monthly on men and women for 1 year under basal metabolic conditions. We took into consideration the phase of the menstrual cycle.

EC was measured in nonanesthetized monkeys under different experimental conditions: with placement on the hands (22 monkeys, 108 tests) with placement in supine position (25 monkeys, 50 tests), in a primatological chair (8 monkeys, 120 tests) and in an adjustable cage (9 monkeys, 96 tests), We studied the seasonal dynamics in the baboons with immobilization in the adjustable cage and in the rhesus monkeys while keeping them constantly in the primatological chair.

A comparison was made of topography of the tested zones of the skin on the limbs in man and monkeys by the anatomical and x-ray method. For this purpose, we first identified the standard skin zones according to conventional anatomical reference points and test for maximum electric conductivity of these zones performed with standard instruments. The identified points were marked with metal pushpins in order to obtain a contrast image on x-rays. X-rays of the limbs were taken in the anteroposterior projection from the lateral and mesial aspects.

Results and Discussion

The results of our tests revealed that there was virtually complete anatomical homology in topography of skin zones with maximum EC on the limbs of man and monkeys. As can be seen in Figure 1, the zones are projected on identical segments of extermital bones of man and monkeys. This is attributable to the fact that the hand and foot of monkeys were anatomically more differentiated than in other animals. The latter is reflected in maximum anatomical similarity of topography of muscular and vascular systems, and peripheral nerves of the extremities of man and this species of animals [5, 8, 10]. The demonstrated anatomical and topographic homology of systems of tested AZS served as the basis for comparing the functional characteristics of these zones in man and monkeys with respect to the main characteristics of ECP.

The averaged EC profiles of healthy men and women were characterized by virtually the same EC in tested skin zones of the limbs. This was reflected in the relatively symmetrical form of ECP (Figure 2). The absence of marked lateral and transverse asymmetry of EC values (asymmetry parameters ranged

from 0.8 to 1.1) is indicative of similar general functional characteristics of skin zones of the human limbs. However, it should be noted that the parameter of uniformity of distribution (ΔEC) ranged from 7 to 30 μA. This is indicative of considerable differences between individual AZS according to local EC parameter.

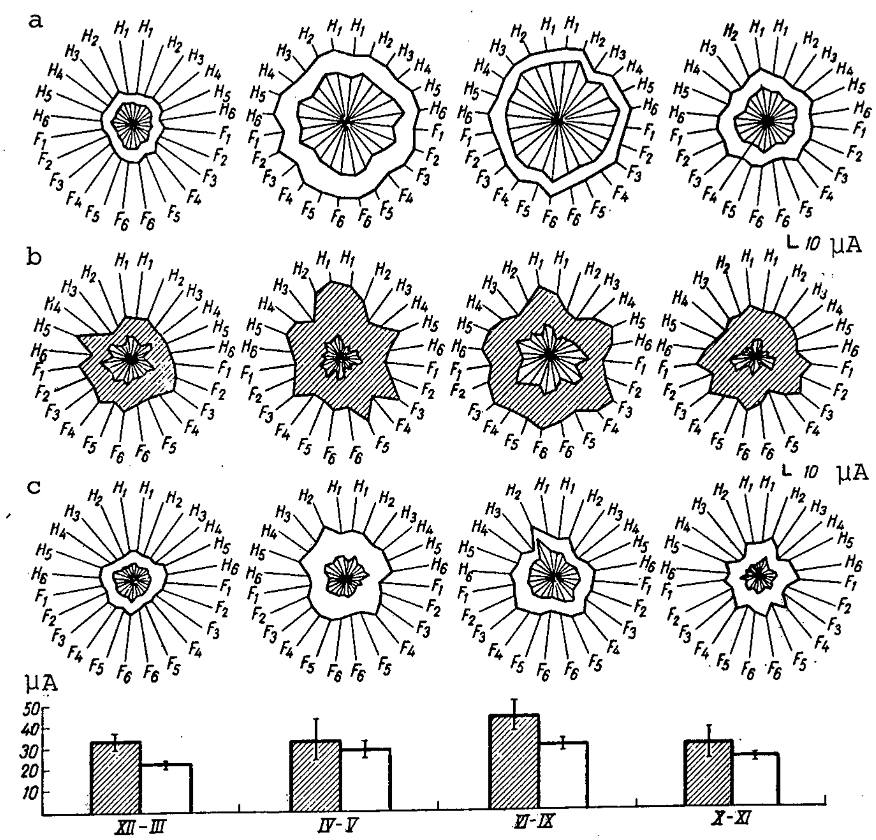


Figure 2. ECP in men (a) and women in first (b) and second (c) phases of menstrual cycle in the four seasonal periods

Here and in Figure 3: Roman numerals refer to months. ECP given in the form of 95% confidence zone of means for different AZS. Bottom: EC in women for first (striped bars) and second (white bars) phases of menstrual cycle.

Analysis of the findings revealed substantial seasonal changes in ECP, which showed a high degree of correlation (r = 0.84, P 0.01) with mean monthly air temperature according to parameter of mean EC ($\overline{EC}$). In addition, it should be noted that no reliable correlation was demonstrable between characteristics of ECP, barometric pressure and air humidity. In view of the marked correlation between $\overline{EC}$ and air temperature, ECP characteristics were compared for the following seasonal samples: December-March (XII-III), April-May (IV-V), June-September (VI-IX) and October-November (X-XI). It should be noted that a seasonal rhythm of ECP changes was well-demonstrable in both men and women. In the latter, it was demonstrable rather distinctly for the first and second phases of the menstrual cycle (see Figure 2). However, the

appreciable differences in $\overline{EC}$ at different periods of hormonal changes in women made it necessary to compare ECP separately for the two phases of the menstrual cycle.

With reference to the general seasonal dynamics of ECP changes in men and women, it should be noted that mean EC was substantially lower (narrowing of ECP) in the winter than in the summer (widening of ECP). In transitional seasonal periods (spring, fall), ECP fell into the intermediate range (see Figure 2).

We found a distinct difference in men between minimal EC in the winter (25.0±0.5 μA) and maximal in the summer (60.0±0.7 μA)(P<0.001). ΔEC ranged from 10 to 22 μA in different periods, combined with minimum variations of all coefficients of ECP asymmetry (from 0.8 to 1.0). In women, there were distinct seasonal dynamics <u>for</u> phase I of the menstrual cycle; however, un<u>like</u> men, they presented minimal $\overline{EC}$ (23.0±2.1 μA) in the fall, whereas maximal $\overline{EC}$ (45.0±2.2 μA) coincided with the season for men. It should be noted that ΔEC fluctuated over a considerably wider range (from 7 to 30 μA) in women, and there was somewhat greater variability of asymmetry coefficients (from 0.8 to 1.1). Although the typical direction of seasonal changes in ECP was demonstrable <u>in</u> the second phase of the menstrual cycle, the differences between minimal $\overline{EC}$ in the winter (22.0±2.0 μA) and maximal in the summer (31.0±2.2 μA) were less marked. On the whole, in spite of the qualitatively similar direction of changes in all periods, ECP characteristics of men and women differed appreciably. This is indicative, to some extent, of difference in reactivity of the autonomic nervous system, reflected in the sex-related distinctions in seasonal condition of autonomic functions of men and women.

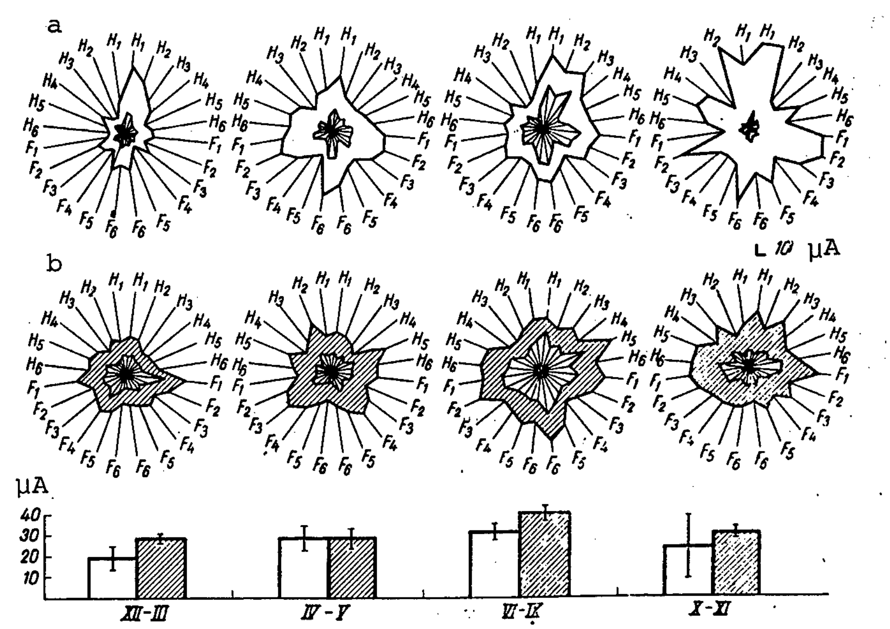


Figure 3. <u>ECP</u> in Macaca rhesus (a) and hamadryas baboons (b), and $\overline{EC}$ (bottom) for the four seasonal periods. Other designations are the same as in Figure 2.

Proceeding from the appreciable seasonal differences in electrodermal conductivity, ECP in man was compared to the two species of monkeys in the corresponding seasons. The general appearance of ECP of Macaca rhesus and hamadryas babbons coincides significantly with the one for man, and it is characterized by an analogous direction of changes (Figure 3). The seasonal distribution of minimum and maximum $\overline{EC}$ of baboons and rhesus monkeys coincided with the data for man. It should be noted that there were no differences between ECP for men, women, baboons and rhesus monkeys according to seasonal minimal $\overline{EC}$. Reliable differences were noted in seasonal maximum for ECP between men and women ($P<0.001$), men and babbons ($P<0.001$), men and Macaca rhesus ($P<0.001$). Seasonal maximum $\overline{EC}$ (41.0±2.0 μA) of baboons did not differ from the one for women in the first phase of the menstrual cycle and was reliable higher in the second phase ($P<0.001$). Conversely, for rhesus monkeys this parameter did not differ from ECP of women in the second phase of the menstrual cycle and was reliably lower in the first phase ($P<0.01$).

Table 1. Seasonal dynamics of main characteristics of EC profile in man and monkeys

Object	Season (months) XII–III					IV–V				
	$\overline{EC}$	ΔEC	d/s	H/F	i/e	$\overline{EC}$	ΔEC	d/s	H/F	i/e
Men	25,0±0,5	10,0±0,4	0,9	0,8	0,9	56,0±1,0	15,0±0,9	1,0	1,0	1,0
P_1	<0,01	<0,001				<0,001	<0,05			
P_2	<0,05	<0,01				<0,001	<0,05			
Women										
phase I	33,0±2,2	17,0±1,6	0,9	1,0	1,0	34,0±2,4	22,0±3,9	0,9	0,9	0,9
phase II	22,0±2,0	8,0±0,4	0,8	1,0	1,0	29,0±2,3	16,0±1,5	0,9	1,2	1,0
P	<0,01	<0,001				>0,05	>0,05			
Baboons	28,0±2,1	31,0±1,4	1,0	0,7	0,8	28,0±2,1	20±2	1,0	0,9	0,9
Macaca	22,0±2,2	34,0±3,1	1,3	1,2	0,8	28,0±2,1	32±3	1,1	0,8	0,9
P	<0,05	>0,05				<0,01				

Object	Season (months) VI–IX					X–XI					$P_{\overline{EC}}$
	$\overline{EC}$	ΔEC	d/s	H/F	i/e	$\overline{EC}$	ΔEC	d/s	H/F	i/e	
Men	60,0±0,7	19,0±0,7	1,0	1,0	1,0	37,0±1,3	22,0±1,3	0,9	1,0	1,0	<0,001
P_1	<0,001	<0,01				<0,001	<0,001				
P_2	<0,001	<0,01				<0,05	>0,05				
Women											
phase I	45,0±2,2	30,0±2,9	0,9	0,8	1,1	23,0±2,1	7,0±0,6	1,1	0,8	0,9	<0,001
phase II	31,0±2,1	25,0±1,2	0,9	0,9	1,0	30,0±2,2	20,0±3,0	0,9	0,8	0,8	<0,01
P	<0,01	>0,05				<0,05	<0,01				
Baboons	41,0±2,1	32,0±1,8	1,1	0,9	1,0	30,0±2,2	25,0±2,5	1,0	0,9	0,9	>0,05
Macaca	34,0±1,9	38,0±1,9	1,4	1,0	0,8	28,0±2,4	38,0±6,7	1,1	0,9	0,8	<0,001
P	<0,05	<0,05				>0,05	>0,05				

Note: $P_{\overline{EC}}$ is reliability of differences between seasonal maximum and minimum (EC), P_1 and P_2 is the same between men and women in first and second phases of menstrual cycle, respectively.

Seasonal minimal and maximal $\overline{EC}$ was reliably lower in rhesus monkeys than in baboons (Table 1). However, it should be noted that, on the whole, seasonal dynamics of changes in ECP characteristics were more prominent in the former

than in baboons. In the latter, in spite of the typically same direction of change, the difference between seasonal maximum and minimum $\overline{EC}$ was unreliable, whereas in rhesus monkeys reliable differences were demonstrated between these ECP characteristics (see Table 1).

A distinction of simian ECP was the more marked differences between EC in different AZS. For this reason, ΔEC was considerably higher than in men and women (see Table 1). ΔEC ranged from 20 to 32 μA in different seasons in baboons and from 33 to 28 μA in rhesus monkeys. This was manifested by less uniform distribution of electrodermal conductivity around the ECP. In this respect, the simian ECP corresponded more to that for women. This can be related, to some extent, to the greater functional lability due to cyclic hormonal activity in women. This is also indicated by the appreciable differences between ECP characteristics of women in different phases of the menstrual cycle. In monkeys, functional lability reflected by uneven distribution of ECP characteristics is apparently related to constant mental and emotional stress due to the anthropogenic factors of the experimental situation.

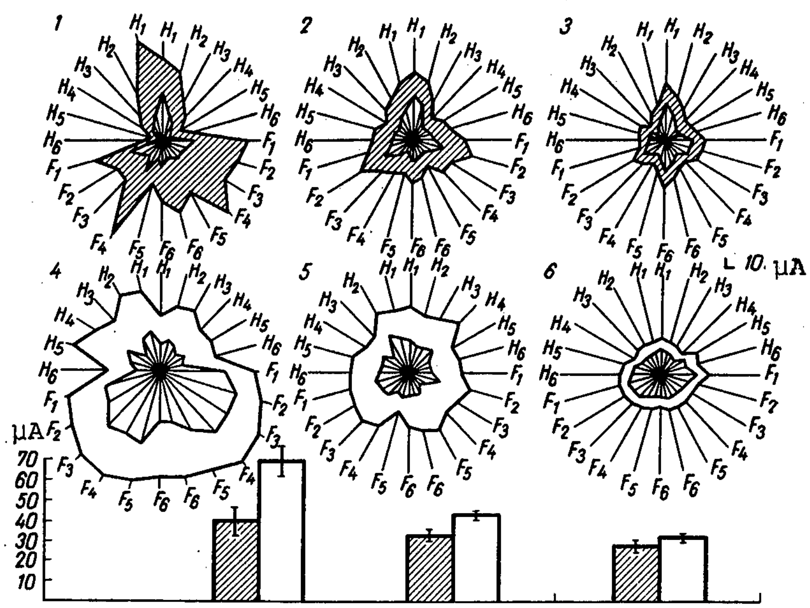


Figure 4. ECP of rhesus (striped areas) and baboons (white) under different immobilization conditions. Bottom--$\overline{EC}$

1, 4) immobilization in horizontal position   3) in primatological chair
2, 5) same with fixation on the hands   4) in adjustable cage

Differences in immobilization of monkeys when measuring EC affected ECP considerably (Figure 4). This must be borne in mind when conducting investigations on these species of animals. Reliable differences in $\overline{EC}$ were demonstrable under all immobilization conditions, in both baboons and rhesus monkeys. It is important to note that species-specific ECP differences persisted. They were manifested under all experimental conditions by higher $\overline{EC}$ for the baboons

(Table 2). Another species-specific difference was the reliably higher ΔEC in Macaca rhesus monkeys.

Table 2. Principal characteristics of ECP of monkeys under different experimental conditions

Object	Type of immobilization														
	supine					on hands					in chair (cage)				
	$\overline{EC}$	ΔEC	d/s	H/F	i/e	$\overline{EC}$	ΔEC	d/s	H/F	i/e	$\overline{EC}$	ΔEC	d/s	H/F	i/e
Baboons	72,0±2,1	70,0±5.7	1,0	0.5	0,9	43,0±2,1	21,0±1,6	1,1	1,0	0,9	32,0±1,0	20,0±0,4	1,0	0,9	0,9
Macaca	40,0±2,2	66,0±6,6	1,1	0,6	0,7	34,0±2,0	31,0±2,0	1,0	0,9	0,7	26,0±1,0	33,0±0,6	1,2	1,0	0,8
P	<0,001	>0,05				<0,05	<0,01				<0,01	<0,001			

When the animals were immobilized in supine position, ΔEC increased significantly, while interspecific differences leveled off. Perhaps this reflects a high functional lability of autonomic functions in the presence of mental and emotional stress due to immobilization. Marked psychoemotional excitement elicits functional changes in the same direction and levels off species-specific differences in ΔEC. However, the latter persisted with $\overline{EC}$ changes: during immobilization $\overline{EC}$ increased by 125% in the baboons and 54% in the rhesus monkeys. This reflects greater psychoemotional reactivity of babbons in response to immobilization. When interpreting the changes in ECP characteristics of monkeys immobilized in supine position, one should also take into consideration the significance of hemodynamic changes related to the animals' clinostatic position.

Sensitivity of ECP to different factors warrants the belief that the method of characteristics of EC profiles may be useful in assessing general condition, psychoemotional reactivity, condition of the autonomic nervous system and such a multifunctional ectosomatic system as the integument, which performs diverse functions. The anatomical and topographic homology of AZS and similar ECP characteristics in man and monkeys apparently indicate that there is the same philogenetic basis for formation of functional characteristics of EC in different species of primates, and justifies the use of monkeys for future investigations of informativeness of this method in diagnosing functional and pathological states.

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UDC: 629.78:616.12-073.97:615.837.5

INTERPRETATION OF RIGHT HEART KINETOCARDIOGRAM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 4 Jul 85) pp 69-71

[Article by V. A. Degtyarev, A. Ya. Kormer, V. A. Rogov, V. Ye. Tolpekin, L. P. Tsyganov, V. N. Ragozin, Ye. Yu. Shcherbakov and Z. A. Kirillova]

[English abstract from source] On the basis of ultrasonic Doppler valvulocardiography of 20 healthy men and catheterization of the right heart of 15 patients with acute large-focal myocardial infarction, the development of elements of the right kinetocardiograms (KCG_r) is explored. Comparison of kinetocardiograms of the right heart with ultrasonic and catheterization data has demonstrated that KCG_r can be used to examine right heart contractions of cosmonauts and pilots in flight and on the ground as well as of patients to diagnose pathologies of the right compartments of the heart.

[Text] Kinetocardiography is used for in-depth examination of cosmonauts during flight [2]. The kinetocardiogram (KCG) was used mainly to study the dynamics of phases of the left heart and rate of propagation of pulse wave over the arteries. No studies were made of the dynamics of contraction of the right heart of cosmonauts, in spite of its great importance, in view of the lack of a validated criterion for identifying phases of the cardiac cycle on the KCG recorded over the right heart (KCGr), as well as inadequate metrological back-up of measurements.

In view of the foregoing, our objective was to define the genesis of KCGr elements. For this purpose we used two control methods: ultrasonic Doppler valvulocardiography (USDVC) and direct catheterization of the right heart and great vessels.

Methods

KCGr was recorded using a piezoceramic sensor at a time constant T = 0.05-0.07 s and frequency band up to 30 Hz, identical to sensors in the Polynome-2M and Aelita equipment used for in-depth examination of cosmonauts aboard Salyut orbital stations. The receiving part of the sensor is a rubber capsule, 4×6 cm in size, filled with porolon [plastic], was placed in the fourth intercostal space to the right of the sternum. We used the numerical nomenclature proposed by L. B. Andreyev [1] to designate KCGr elements.

USDVC was used to pinpoint the pulmonary artery valve (sensor placed in second intercostal space to the right of the sternum) and tricuspid valve (sensor in right intercostal space, less often in fourth intercostal space to the right of the sternum) [4].

The right heart and pulmonary artery were catheterized using two No 9 Cournand catheters. After inserting the first catheter, we successively recorded pressure in the superior vena cava (SVC), right atrium (RA), right ventricle (RV), pulmonary artery (PA) and pulmonary capillaries; then the second catheter was introduced and a simultaneous record was made of pressure curves of the pulmonary artery and right ventricle, right atrium and right ventricle. The pressure sensors were placed on the level of the right atrium. A Mingograph-81 was used to record the tracings at the rate of 50 and 100 mm/s. The USDVC method was used to examine 20 healthy men 18-20 years of age, direct catheterization of the right heart was performed on 15 male patients 46-62 years of age with the diagnosis of acute large-focus myocardial infarction of the left ventricle of different localizations, with onset 1 to 7 days previously. Analysis of pressure curves in the RV and PA, in order to calculate duration of phases of the cardiac cycle, was made by the conventional method of V. L. Karpman and V. S. Savelyev [3].

Results and Discussion

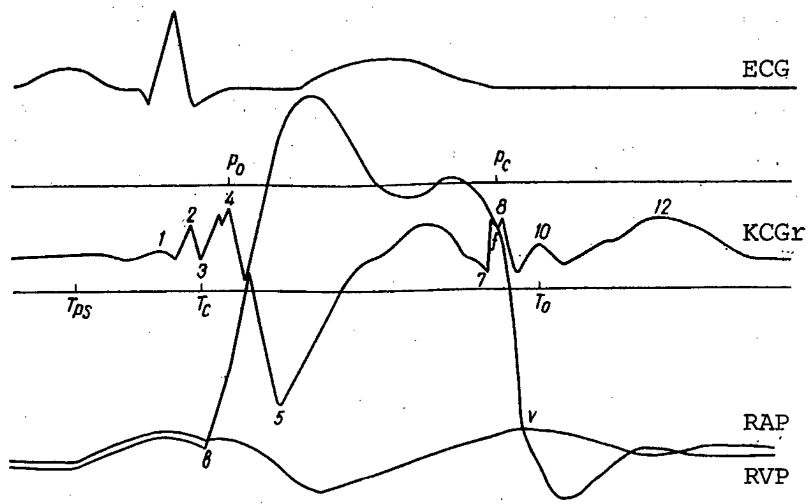
The shape of the KCGr curve differs noticeably from the apical KCG. On the KCGr, after a small atrial wave *1* there are positive waves *2* and *4*, which differ from KCG_1 [left] in considerably lower amplitude, then a relatively deeper negative collapse *5* (see Figure). The ratio of amplitude of wave *4* to that of wave *5* on the KCGr is about 1:3 or 1:4. Unlike the KCGl, in the diastolic part of KCGr, between waves *8* and *12*, in 83% of the cases there is a marked positive wave *10*, which occasionally has a split appearance. Wave *12* on the KCGr is analogous to wave *10* on the KCGl, and it has a notch on the ascending arm. The shape of the KCGr of patients with myocardial infarction differs from the curve for healthy individuals in that the amplitude of positive and negative waves is significantly lower, and there is some smothing of the curve's pattern. For example, wave *10* is demonstrable in only 50% of the cases, and it was impossible to obtain a readable KCGr in 20%.

We consider the cause of this to be age-related changes in the thorax (diminished rigidity of the anterior chest wall, collagenosis of intercostal spaces), pulmonary emphysema, enlargement of the subcutaneous fatty layer, impairment of contractile processes in the weakened and dilated right ventricle.

A comparison of USDVC and KCGr elements revealed that the time that the PA valve opens (P_o) corresponds to the peak of wave *4* on the KCGr, and in the case of splitting, to its second wave. The time of closure of PA valve (P_o [sic]) always corresponds to the notch on the split peak of wave *8*. Opening of the tricuspid valve (T_o) coincides with the peak of wave *10* or its center in the case of splitting.

A comparison of KCG elements to manometric curves of the right heart and PA confirmed the findings. Point *b* on the RV pressure curve--time of closure of the tricuspid valve--corresponds to the peak of negative wave *3* on the KCG.

Point *c* on the PA pressure curve--time of opening of PA valve--and point *f* on the RV pressure curve--time of closure--are projected on the peak of waves *4* and *8* of the KCGr, respectively. The point of intersection of descending RV pressure curve with wave *v* of the RA curve--time T_0--coincides with the apex of wave *10*, and if it is absent, with the bottom point of collapse between waves *8* and *12* on the KCGr. The differences between time intervals determined on the KCGr and other methods (from the ECG Q wave to elements of KCGr and corresponding elements on USDVC and pressure curves) were statistically unreliable, in both healthy subjects and patients with myocardial infarction.



Genesis of KCGr elements according to results of direct manometry of the heart and USDVC. Explained in the text. RAP and RVP--pressure in right atrium and right ventricle, respectively

Duration of systolic phases and period of relaxation of the right ventricle

Phase of cardiac cycle	KCGr*	Direct manometry	
		reference [3]	reference [6]
Tension	0,111±0,004	0,104±0,002	0,08±0,079
Asynchronous contraction	0,077±0,003	0,073±0,001	0,065±0,0087
Isometric contraction	0,032±0,002	0,031±0,001	0,016±0,004
Ejection	0,327±0,004	0,236±0,005	—
Protodiastole		0,037±0,002	—
Isometric relaxation	0,054±0,002	0,047±0,003	—
Interval	0,981±0,03	0,683±0,027	—

*Data obtained in the present investigation.

The duration of systolic phases and relaxation period of the RV in healthy subjects determined according to KCGr, as compared to the data of other authors, is shown in the Table. Duration of periods of tension, as well as asynchronous and isometric contraction was found to be rather close to the data of V. L. Karpman and V. S. Savelyev, which they obtained by direct

manometry of the heart. The existing differences, particularly in duration of ejection period, were probably due to differences in duration of the cardiac cycle. The insignificant differences from the data of other authors are probably attributable to heterogeneity of the tested group of subjects.

In the group of patients with acute myocardial infarction of the left ventricle, we demonstrated extension of the tension period to 0.123±0.004 s for the right ventricle, longer phase of its asynchronous contraction, to 0.085±0.005 s with moderate extension of phase of isometric contraction to 0.037±0.004 s and decrease in ejection period to 0.292±0.004 s (by 17% of nominal value). The phase of isometric relaxation increased to 0.061±0.002 s. The obtained data are consistent with those published previously [5].

Thus, the results of these investigations revealed that the KCGr reflects the dynamics of contraction of the right heart. The method can be recommended for in-depth examination of cosmonauts and pilots on the ground and in flight.

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METHODS

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METHOD OF CALIBRATING OCULOGRAMS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 12 Apr 85) pp 71-73

[Article by B. A. Karpov and L. G. Aleksandrov]

[Text] The recording of eye movements is used extensively in aviation and space psychology and medicine to monitor the condition and actions of people in flight [2]. However, the precision of the conventional method of calibrating oculograms, particularly in the case of remote registration of eye movements without contact, is not high enough.

Traditionally, calibration of oculograms (electrooculograms, as well as recording of eye movements by electromagnetic, electron optical and other methods) co consists of the following. Two calibration markers are placed before the subject symmetrically in relation to the midline, and they are at a strictly specific distance from one another. The subject is instructed to move his eyes from one marker to the other, and the eye movements are recorded. Knowing the distance between markers, the required amplification is set and a calibration tracing is formed, which is used as the scalar gage to interpret the oculogram recorded in the course of subsequent testing. This method of calibration became so popular that the question of calibration is omitted in many publications dealing with human eye movements.

However, it is known that, in the case of voluntary switching of gaze from one stationary fixation point to another, the direction of gaze does not necessarily coincide with the spatial position of the fixation point [1]. The following rule applies: the farther the new target is from the first fixation point, the greater this noncoincidence. For example, with horizontal jumps, the eye movements fall 1.4 and 2.8° short of a target 10 and 20°, respectively, away from the midline [1, p 76]. Hence, such errors may also occur during calibration, which is made on the basis of voluntary saccadic movement of gaze between given markers.

We describe here the results of testing the magnitude of error in voluntary movement of gaze between two stationary calibration points 10° apart in the horizontal plane, as well as a method that eliminates the error.

Methods

The tests were performed on 5 healthy male subjects. Eye movements were recorded by the photographic optic method using a central suction cup by the method of A. L. Yarbus [3]. We calculated the ratio of route traveled by the subject's gaze when moving from one calibration marker to the other to the actual distance between the markers. In cases where the change was made by a series of saccadic movements, the route traveled by the gaze was calculated as the sum of saccadic movements. The results of the tests are listed in Table 1.

Table 1.
Errors when changing fixation point by means of random saccadic eye movements

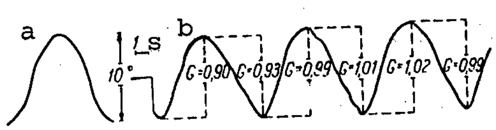
Subject No	G_m	Mean error %	Mean error angular min
1	0,81	—19	—114
2	0,87	—13	—78
3	0,84	—16	—96
4	0,83	—17	—102
5	0,88	—12	—72
Mean values	0,85	—15	—90

Key, here and in Table 2:
G_m) mean relative amplitude of eye movements

Table 2.
Characteristics of smooth tracking eye movements at different frequencies of oscillation of target

Subject No	F	G_m	Mean error %	Mean error ang. min
1	0,13	0,98 (1,4)	—2	—12
2	0,13	1,01 (1,3)	+1	+6
3	0,25	1,00 (1,2)	0,0	0,0
4	0,20	0,98 (1,2)	—2	—12
5	0,20	0,99 (1,2)	—1	—6
Means	—	0,99	—0,80 %	—4,8

Note: F is frequency of oscillation of target (in Hz); numbers of half-periods on the basis of which G_m was calculated are given in parentheses



Tracing of subject's eye movements when tracking calibration target; half-periods are indicated with value of G for each of them (explained in the text)
a) fragment of movement of calibration target: amplitude of oscillations 10°, frequency 0.13 Hz
b) tracing of horizontal component of movements of subject's dominant eye

Apparently, when calibrating the oculogram by means of saccadic eye movements, the obtained scalar standard will be an average of 15% lower than the given distance, which would also lead to error in evaluating the tracing of eye movements in the subsequent test.

In order to reduce appreciably the error that arises with traditional calibration, one should replace the random movement of gaze upon the calibration markers with smooth tracking eye movements. It was previously shown that if an individual fixes his gaze on targets that move smoothly in accordance with a predictable law (for example, sinusoidal at a frequency of

less than 1 Hz), the accuracy of fixing the eyes on the target is close to 6-8', and it persists over a rather wide range of amplitudes of eye movements [4].

The proposed method amounts essentially to the following. There is a test field in front of the subject (a screen or projection perimeter, in the center of which is a target that can be put into oscillating pendulum-like motion at a specified frequency and amplitude, and in a specified plane. There are two stationary calibration markers to the right and left of this target (we shall call it a moving target), the distance between which is specified in accordance with the scale of the tracing and required calibration precision. In order to obtain a calibration signal, the moving target is put into pendulum-like oscillatory motion at an amplitude that equals the distance between the stationary calibration markers. The frequency of target oscillations must be in the range of 0.1-0.25 Hz. The subject is instructed to track the moving target, and 4-5 periods of tracking eye movements are recorded. On the obtained tracing, all distances between neighboring points of eye movement are measured for each tracking half-period (see Figure). One chooses 2-3 maximum distances between points of eye reversal and their mean is used as the scalar standard.

We submit below the results of testing the accuracy of the scalar standard, which was obtained with use of the proposed calibration method at different frequencies of target oscillation (distance between calibration markers is 10°). The proposed method was tested on five healthy subjects. The results are listed in Table 2.

Table 3. Values for G when tracking oscillating target moving between two calibration points

Subject No	Distance between calibrat. points, °	Oscillation frequency, Hz	Half-period								
			1	2	3	4	5	6	7	8	9
1	5,5	0,20	1,00	1,01	1,00	0,96	0,96	0,96	0,91	0,96	0,99
2	5,5	0,40	0,99	1,00	0,92	0,91	0,96	0,96	0,86	0,87	0,94
3	10	0,13	0,98	0,95	0,91	0,98	0,86	0,91	0,87	0,89	0,88
4	10	0,13	0,99	1,01	1,02	0,99	0,95	0,96	0,95	0,95	0,95
5	10	0,20	0,98	0,97	0,85	0,93	0,85	0,95	0,88	0,80	0,80
6	10	0,40	0,99	1,02	0,75	0,83	0,86	0,79	0,86	0,91	0,82
7	10	0,20	0,99	0,98	0,91	0,88	0,91	0,89	0,87	0,95	0,85
8	6,2	0,40	1,01	0,97	0,82	0,84	0,88	0,80	0,89	0,77	0,84
9	6,2	0,20	0,99	0,81	0,78	0,82	0,81	0,93	0,90	0,84	0,84

A comparison of the accuracy of calibration by means of random saccadic and smooth tracking eye movements on the basis of data in Tables 1 and 2 shows that the proposed method yields a mean margin of error that is lower by a factor of 10 (1-2%) than the traditional calibration method.

The results of a special study revealed that the amplitude of tracking eye movements is not constant; it is closest to the amplitude of movement of the target in the 1st-4th half-periods of tracking it. Thereafter, due to

increase in role of the mechanism of adopting the rhythm, the amplitude of tracking eye movements gradually drops. However, among the first few half-periods one can always find some that are the closest to a specified amplitude. One can see this from the results of special investigations, which are listed in Table 3.

The proposed method of calibrating oculograms is particularly effective when testing low-amplitude oculomotor reactions of individuals, when a precise evaluation of amplitudes of eye movements is required.

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RHEOTACHOOSCILLOGRAPHIC RECORDING OF SIMIAN BLOOD PRESSURE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
Vol 20, No 3, May-Jun 86 (manuscript received 18 Apr 85) pp 73-75

[Article by A. N. Demin, M. V. Galustyan, G. S. Belkaniya and V. A. Dartsmeliya]

[Text] Noninvasive methods (tachooscillography and phonotachooscillography) of measuring arterial pressure (BP) are gaining wide clinical application [3]. However, major difficulties are involved in using these methods on experimental animals (in particular, monkeys), due to their small extremities, presence of pelage, need to use standard ultrasonic, phono- and piezometric pulse sensors.

A noninvasive method of measuring systolic, mean dynamic and diastolic BP in monkeys in the course of experiments is proposed, which is based on recording the rheooscillogram, in order to objectivize readings and make precise determination of these parameters.

An expandable cuff from a sphygmomanometer and electrodes to record rheooscillograms of extremital vessels are applied to the limb of the monkey. Figure 1 illustrates placement of active and measuring electrodes. The rheotachooscillogram is recorded during smooth compression and decompression of the cuff, which is on the arm, thigh or lower leg, using an RPG2-02 rheoplethysmograph by the method of tetrapolar rheography. Any standard recording device can be used to record the rheotachooscillogram. Smooth compression and decompression are produced by including an airtight container (see Figure 1) in the manometer system.

When recording tachooscillograms on a domestically produced electrocardiograph, discrete pressure levels in the cuff can be marked at intervals of 10 mm Hg on the recording instrument in accordance with visual reading of pressure values on the sphygmomanometer dial (Figure 2, top). In addition, it is possible to record pressure in the cuff continuously using a standard electromanometer connected in parallel with the membrane sphygmomanometer. In this case, the signal is calibrated for pressure using a standard method. A parallel tracing of the rheooscillogram and pressure is made on the recorder (Figure 2, bottom).

The obtained graphic tracings of rheotachooscillographic signals are interpreted according to known signs, including the method of measuring mean BP according to degeneration of dicrotic formation of rheooscillations [2]. In

our set-up for measuring BP during smooth decompression, reverse dynamics are taken into consideration--appearance of dicrotic element of rheooscillations. It is desirable to use this mode on animals, since compression of the limb could be associated with muscle tension, which affects the quality of the rheotachooscillogram.

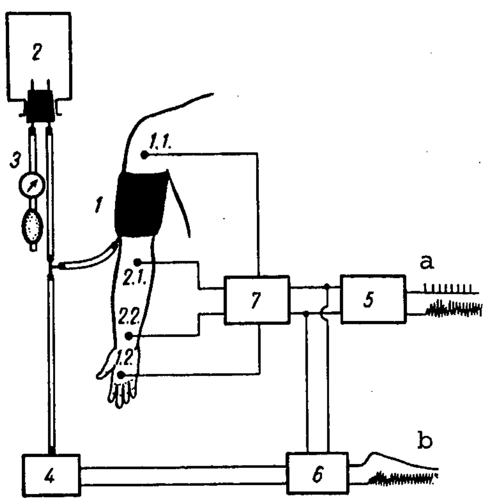

Figure 1.
Diagram of BP measurement by rheotachooscillographic method with discrete (a) and continuous (2) recording of pressure in pneumatic cuff

1) cuff
2) airtight container
3) membrane sphygmomanometer
4) electric manometer
5) electrocardiograph
6) recording
7) rheoplethysmograph

1,1 and 1,2) active [current] electrodes
2,1 and 2,2) potential electrodes of rheoplethysmograph

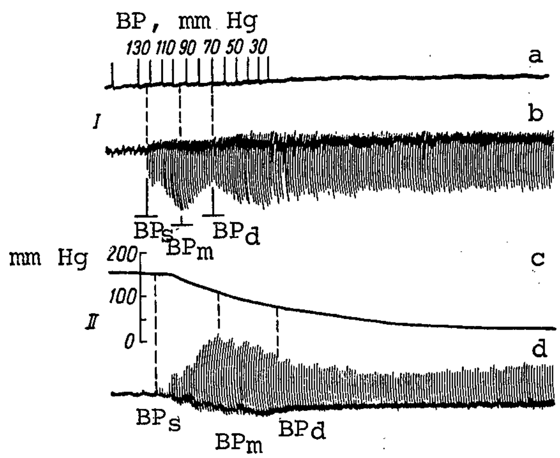

Figure 2.
Rheotachooscillograms of monkeys with discrete (I) and continuous (II) recording of pressure in pneumatic cuff

Here and in Figure 3:
a) decompression mode mark
b) rheotachooscillograms of BP_s, BP_d and BP_m, 124, 72 and 94 mm Hg, respectively in I, 150, 75 and 108 mm Hg in II

The arterial rheotachooscillogram reflects in the first derivative of the basic rheogram the pulsed changes in delivery of blood to tissues, which changes due to changing correlation between pressure in arteries and counterpressure in the cuff. Such a rheooscillogram, which is recorded during smooth compression and decompression, is an objective record that shows systolic (BP_s), mean dyanmic (BP_m) and diastolic (BP_d) blood pressure. The abrupt increase in amplitude of oscillations during decompression and its decline when pressure in the cuff equals BP_d serve as indicators of these parameters. Cuff pressure at which amplitude oscillations appear on the rheotachooscillogram corresponds to BP_s. The widest scatter of amplitude of rheooscillations corresponds to BP_m, and a decrease in amplitude reflects BP_d parameters (see Figures 2 and 3).

Figures 2 (top) and 3 clearly show the graphic reflection of dynamics of appearance of dicrotic element of rheooscillations. The dicrotic notch is

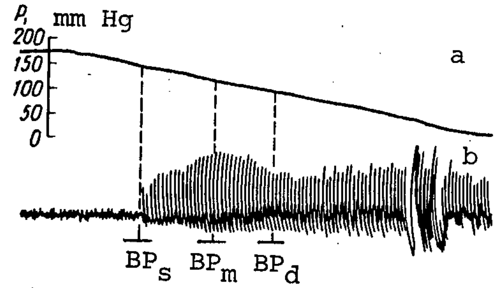

Figure 3.
Dynamics of dicrotic element of rheooscillations during smooth decompression of pneumatic cuff, recorded at increased tape feeding rate; arrowhead shows pressure in cuff

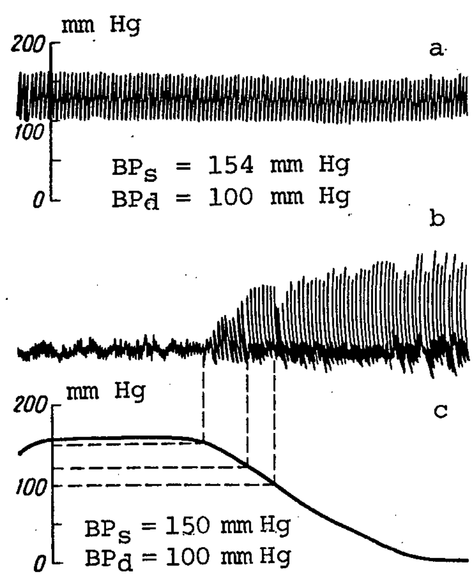

Figure 4.
Parallel recording of BP by direct (a) and rheotachooscillographic (b) method; c--mark for mode of decompression in pneumatic cuff. BP_s and BP_d 154 and 100 mm Hg in (a), 150 and 100 mm Hg, respectively, in (b)

directed toward the basic oscillation, its appearance and further build-up coincide with a level corresponding to BP_m. Maximum amplitude of the dicrotic part of the rheooscillations coincides with the level of BP_d. There are also physical conditions that correspond to this phenomenon--restoration of patency of great vessels of the limb. In a number of instances, when identifying BP_d level one can use as a guide the dynamics of the rheooscillation notch oriented in the opposite direction from the basic one and dicrotic oscillation. This notch appears on the rheotachooscillogram corresponding to BP_d.

Depending on the different conditions of recording BP by the proposed method, determination can be made on the rheotachooscillogram of either all the listed parameters or only some of them. Sometimes it is possible to accurately determine only BP_s and BP_m. In such cases, if necessary, it is valid to calculate BP_d from the known condition:

$$BP_m = BP_d + 0.42\,(BP_s - BP_d),$$

hence,

$$BP = \frac{BPm - 0.42BPs}{0.58}$$

In order to verify the data obtained by the rheotachooscillographic method, we made a parallel recording of BP by a direct method with catheterization of the brachial artery. The recording was made using the manometric unit of the Salyut polygraph. As can be seen in Figure 4, BP measured by the rheotachooscillographic and direct methods was the same.

The positive element in the rheotachooscillographic method of measuring BP is that in combined rheographic studies it can be combined with measurement of basic parameters of central hemodynamics (stroke and minute output, total peripheral vascular resistance) by the method of tetrapolar thoracic rheography [1]. Methodologically, rheotachooscillography is simple, and it can be automated at the stages of measurement and processing of rheotachooscillograms. It is desirable to use the

rheotachooscillography to measure BP in chronic experiments on any animal species with or without immobilization. This circumstance enables us to recommend the method developed for measuring BP in the program of preparations for and performance of experiments aboard biosatellites with the use of monkeys.

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RAT CAGE FOR SIMULATION OF LONG-TERM HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
Vol 20, No 3, May-Jun 86 (manuscript received 8 Apr 85) pp 75-78

[Article by A. I. Gritsuk and I. G. Danilova]

[Text] Investigation of the problem of hypokinesia (HK) is of interest to a wide circle of specialists. Its successful development depends largely on choice of an adequate model. At the present time, various methods have been described [6, 12] for partial and complete immobilization of animals: tenotomy, immobilizing bandages; plaster cast, immobilization of the limb or tail, suspension in belly hammocks, small cages, etc.

These immobilization methods differ in degree of "rigidity," and they permit simulation of different effects of HK and weightlessness. The choice of immobilization method depends on the purposes of experiments. For example, in ground-based studies of biological effects of weightlessness, it would be more effective to keep animals in individual subperitoneal hammocks which reduces entirely muscular exertion, including that used to maintain the body's position. However, this immobilizes an animal for a brief time.

Simulation of HK by keeping animals in small cages has gained wide use. This method does not provide total immobilization, but nevertheless it is minimally traumatic and makes it possible to submit animals to HK differing in rigidity for a long period of time.

Analysis of the literature, which is reflected the most completely in recently published monographs [6, 12], as well as our own experience, convinced us that the design of cages used to simulate long-term HK in animals must meet the following basic requirements: 1) it must enable the animal to maintain a natural position and to groom different parts of its body, which reduces to a significant extent the stressor effect of HK [11]; 2) degree of rigidity of HK must be controllable by means of altering the size of the cage in accordance with the size of the animal; 3) it must be economical, simple to manufacture and use (natural ventilation, delivery of water and feed, collection of excrements), and provide for long-term observation of the animal's general condition and appearance; 4) the material of which the cages are made must be hygienic, mechanically sturdy and chemically inert; it must have good heat-insulating properties. The latter must be considered in particular when working

with animals such as white rats. They have intensive gas and energy metabolism, and rather active muscles, which permits comprehensive demonstration of metabolic distinctions during HK [5]. White rats have deficient thermogenesis and are readily susceptible to overcooling. In the case of prolonged immobilization, when the contribution of muscular thermogenesis to the body's overall heat balance is reduced, the additional increase in heat transfer due to the animal's contact with heat-transmitting cage material could stimulate cold dissociation and distort processes of oxidative phosphorylation.

For this reason, a simple design was developed for a cage to simulate long-term HK in rats, in which the above requirements were taken into consideration (Figure 1).

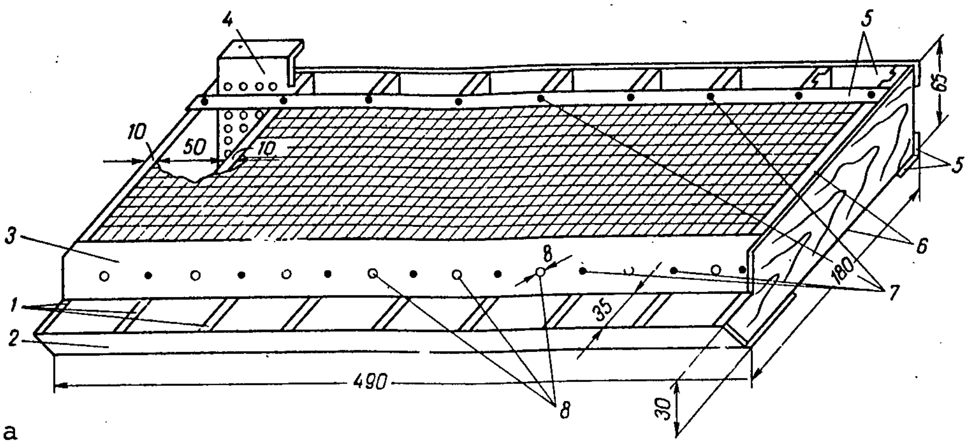
Wood is the main construction material in the cage; it is hygienic, mechanically sturdy and is notable for good insulating properties. A cage for 8 animals is 490×180×65 mm in size, and it consists of wood partitions *1* attached to one another by wood screws *7* in a shell consisting of the following aluminum parts: trough *2*, front panel *3*, strips *5* and *6*. The bottom of the cage is covered with a metal screen with 2×10 mm mesh size. On front panel *3* there are 8-mm openings *8* for feeders in the center of each individual cage. The back wall of the cages is shut by perforated flat aluminum doors *4*, which are inserted in the vertical grooves of the wooden partitions.

The individual cage dimensions, 145×50×65 mm, allow for restricting movements in all directions. At the same time, the experimental animal can assume a natural position and groom different parts of its body. When necessary, the dimensions of the individual cages can be reduced using special wood inserts.

The cages are placed on aluminum or viniplast [vinyl plastic] trays that are 540×220×30 mm in size. The presence of wood shavings on the tray provides for good heat insulation, convenience and simplicity of animal care. The biologically active substances contained in the sawdust provide a good microclimate in the cage. When it is necessary to collect excrements, the cages are placed on a perforated tray, which permits separate collection of feces and urine. Dry feed is supplied in individual feeders formed by the little trough and wood partitions. A wooden plate is installed on the front panel on which 30-50 mℓ water dispenses are secured with a rubber band.

This design is simple to manufacture, reliable and convenient for use, and permits simulation of HK for over a year.

The results of polarographic studies of tissue respiration and oxidative phosphorylation of muscle tissue sections, which were conducted on an LP-7 polarograph (CSSR) in Hanks' medium using a closed platinum Clarke electrode, as well as data on glucose and total lipid levels in blood of animals submitted to HK for up to 140 days, can be used as criteria of adequacy of this model of HK [3]. Changes in the same direction were demonstrated for the myocardium and gastrocnemius muscle with respect to respiration rate of sections on endogenous substrates, which is manifested in the form of significant elevation of this parameter on the 30th, 45th and 70th days of HK, with subsequent decline on the 140th day (see Table). Inhibition analysis (use of sodium amytal, which is an inhibitor of the first segment of the respiratory chain, and sodium



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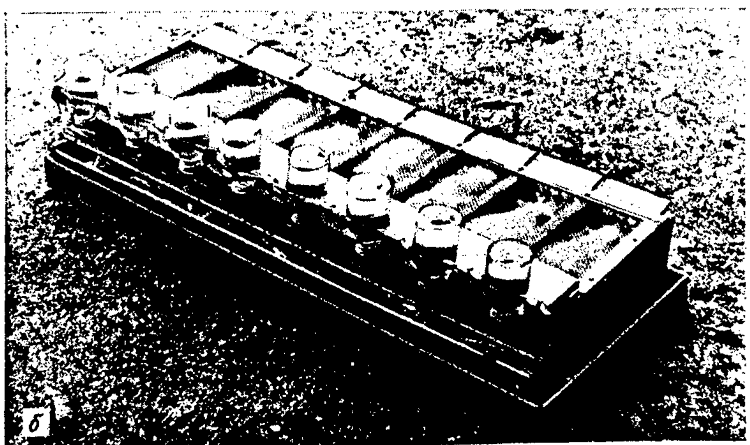

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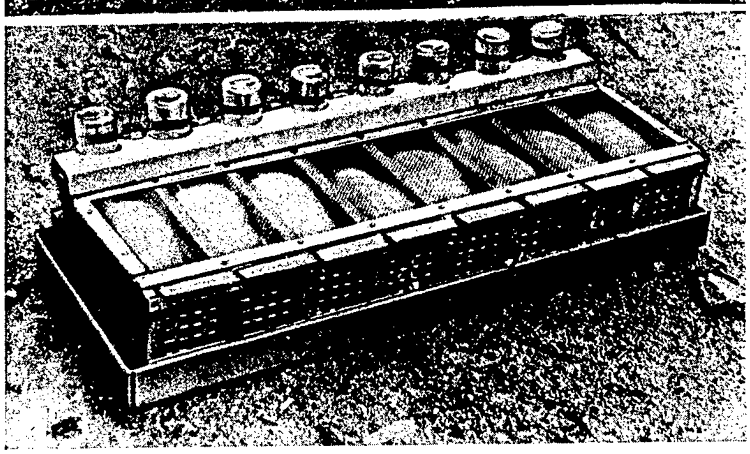

c

Figure 1. Cage for rats
a) diagram of shell with indication of dimensions (in mm; explained in the text)
b) general front view of cage
c) general rear view

malonate, which is an inhibitor of succinate dehydrogenase) was performed to determine the causes of increased rate of endogenous respiration, and the results demonstrated convincingly that there is intensive oxidation of endogenous fatty acids in muscle tissue [3]. Fatty acids, being powerful dissociative agents, attenuate conjugation of oxidative phosphorulation as determined by the magnitude of stimulating effect of 2,4-dinitrophenol (RR_{DNP}--ratio of respiration rate of preparation in the presence of dissociative agent--2,4-dinitrophenol--to respiration rate without this agent). The consistent decline of this parameter for the gastrocnemius is indicative of dissociation of oxidative phosphorylation, which is the principal mechanism for increasing the rate of endogenous respiration of muscle tissue with 30-70-day HK. These data agree well with the described phenomenon of increased oxygen uptake by immobilized rats and increased rate of local oxygen uptake by muscles of the hind limbs of rats on the 79th-170th days of HK [2]. Other authors [6, 9, 10] have demonstrated dissociation of oxidative phosphorylation in the form of decline of P/0 ratio in rat skeletal muscles and myocardium with 45, 60 and 120 days of immobilization.

Effect of long-term HK on parameters of tissue respiration on rat myocardium and gastrocnemius muscle sections (M±m, n = 6-18)

HK, days	Endogenous RR (in "natoms" [atomic mass nano-units?]/mg protein per minute)		Stimulating effect of 2,3-DNP on respiration of gastrocnemius
	myocardium	gastrocnemius	
Control	4,16±0,24	2,95±0,17	1,29±0,06
30	6,83±0,60*	5,20±0,63*	1,24±0,07
45	5,60±0,60*	4,04±0,32*	1,03±0,03*
70	5,13±0,32*	3,72±0,30*	0,98±0,13*
140	3,40±0,23*	2,50±0,20*	0,94±0,05*

*P<0.01-0.05, as compared to control

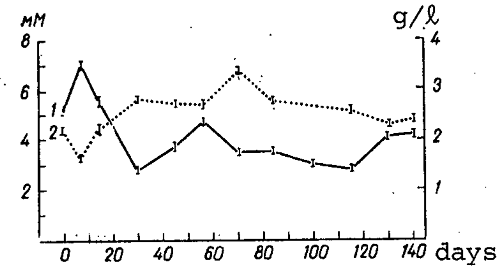

Figure 2.
Effect of long-term HK on blood substrate levels
X-axis, duration of HK (days), y-axis, glucose concentration (1) on the left, total lipids (2) on the right

The same pattern of changes in tissue respiration of muscle tissue of immobilized animals could be due to change in substrate spectrum of blood. Investigation of this question revealed that the correlation between concentrations of glucose and total lipids in blood plasma (Figure 2) can be described on the basis of Rendle's conception of the fat and carbohydrate cycle [8].

Elevation of glucose level on the 1st-14th days is due to mobilization of glycogen [1, 13], whereas subsequent hyperlipemia on the 30th-70th and later days is attributable to intensification of lipolytic activity of fatty tissue [7]. Mobilization of glycogen and activation of lipolysis are apparently initiated by catecholamines, the levels of which remain high up to the 170th day of HK [4]. There are analogous data in the literature concerning level of glycemia [13] and concentration of free fatty acids in blood of animals submitted to HK of various duration [7]. The demonstrated correspondence between hyperlipemia and intense consumption of lipids by muscle tissue confirms the existing

opinion that there is a direct relationship between amount of substrate in blood and rate of its utilization by tissues.

Thus, the data obtained using the above-described model are consistent with the conventional conceptions of metabolic disturbances associated with immobilization [5]. This warrants the belief that the proposed model of HK can be used for investigation of various biological effects of HK.

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BRIEF REPORTS

UDC: 629.78:575.224.23]-019-08

FUNCTIONAL AND STRUCTURAL TRANSFORMATIONS OF CHROMOSOMES IN DIFFERENT PROLIFERATIVE HEMOPOIETIC CELLS IN WHITE RAT BONE MARROW

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 13 Jun 85) pp 78-80

[Article by L. I. Chabala]

[Text] Morphological change in chromosomes due to variation in number of arms was first described in rats [8]. At the present time, intrapopulation polymorphism referable to three pairs of autosomes is observed in laboratory albino and gray rats (Rattus norvegicus) who have a constant diploid number of chromosomes--42 [6, 12, 14]. Elongation of the arms in some chromosomes of rats and other mammalian species were often attributed to pericentric inversions [10-12, 14] or appearance of additional heterochromatin units [3, 7, 9].

We shall discuss here the polymorphism of chromosomes in white rat bone marrow tissue, which we discovered for the first time, their functional and structural transformations in different proliferative hemopoietic cells.

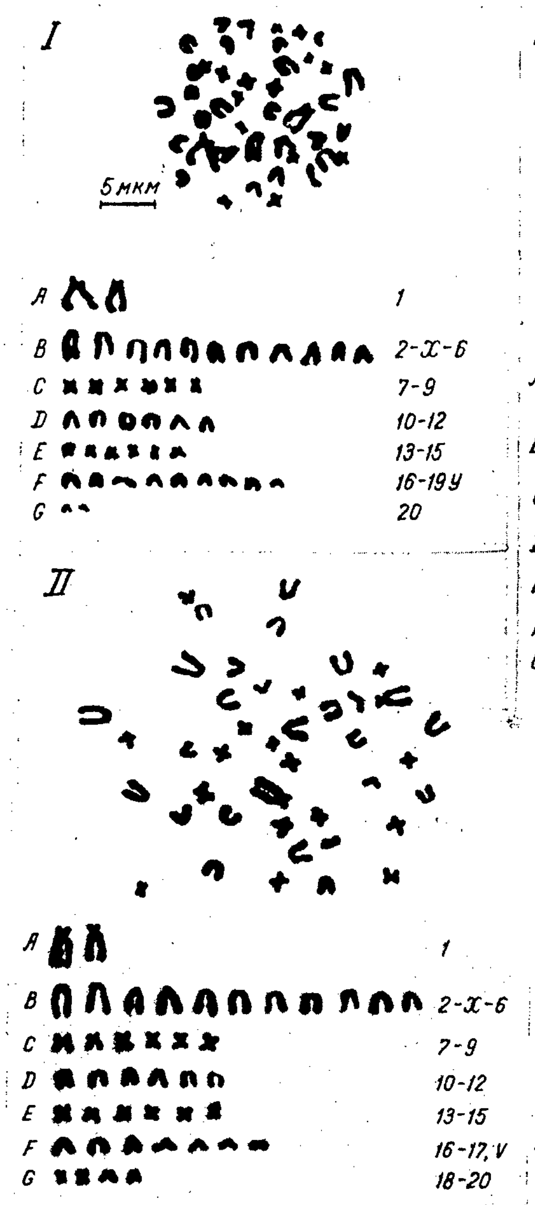
Methods

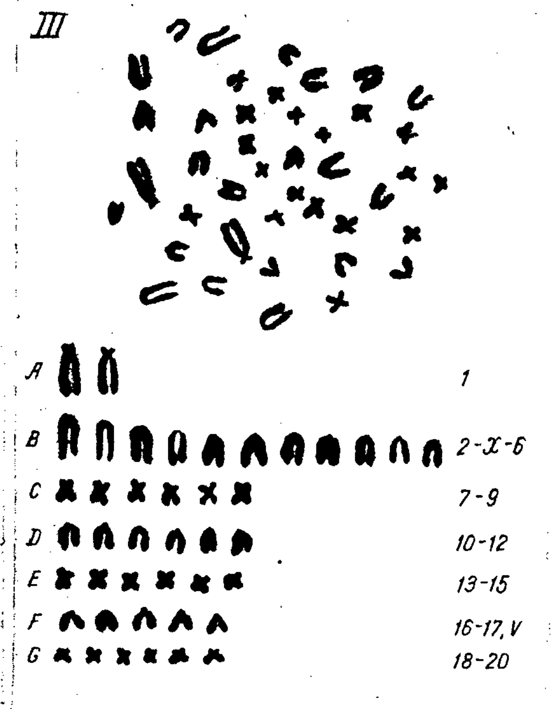
The studies were conducted on male mongrel white rats from the White Moss Vivarium of Laboratory Animals of the USSR Academy of Medical Sciences: on control rats on the 5th day after removal of the spleen and on the 6th day after intermittent hypoxia in a pressure chamber. A total of 41 animals were used in the experiments.

We examined the quantity, morphology, dimensions of chromosomes in bone marrow cells and peripheral blood, as well as mitotic activity and morphology of bone marrow cells using conventional methods [1, 5]. An MBB-1 microscope was used to analyze micropreparations; a microphoto attachment with a Zenith camera was used to take photos at a magnification of 90× for the lens, 1.30 for the app. and 15 for the eyepiece.

Results and Discussion

A total of 1041 metaphase plates with good scatter of chromosomes were analyzed on micropreparations prepared by the standard methods and stained uniformly.





Structural organization of chromosomes: type I (a; in megakaryocyte class), II (б; in lymphatic class) and III (в; in erythroid class) from bone marrow cells of control white rats. Scale--5 μm; on the right--numbers of pairs in each group of chromosomes

We karyotyped 79 typical metaphase plates from the control males, 63 of which were taken from bone marrow and 16, from a culture of peripheral blood. The chromosomes (20 pairs of autosomes and sex XY) were arbitrarily divided into 7 groups (A-G) in order of diminishing size with consideration of shape, and we also took into consideration that X was the larger acrocentric chromosome and Y the smallest acrocentric one [13].

In the rats examined, we also observed polymorphism of the above-mentioned three pairs of autosomes, but on the tissular, rather than population, level. In the two smaller pairs of autosomes there were functional and structural transformations due to the type of hemopoietic cell. These autosomes are referred to as

pairs 18 and 19, in accordance with the classification we adopted. Due to changes in their arm length in F groups, where the smallest acrocentric chromosomes, and G, which contains the smallest metacentric and similar chromosomes, we observed variation of their number. According to this character, each specimen had three types of structural organization of chromosomes in cells, according to number of pairs in group G they were designated as type I, II and III (see Figure). Analysis of the data revealed that under normal conditions there was most frequent proliferation in animal bone marrow of cells with type II structural organization of chromosomes (43.8±1.21%) and least of all, type I (19.9±0.86%).

But we demonstrated only one type II structural and morphological organization of chromosomes from the peripheral blood culture of a male animal. It was established that erythrocytes and thrombocytes have no nuclei in mammalian peripheral blood, and only lymphocytes [5], in the class of white blood cells are capable of division. For this reason, type II structural organization of chromosomes, where pairs 19 and 20 are metacentric and 18 are acrocentric, determines lymphocytes of white blood in rats.

It is known that intensified thrombocytopoiesis is observed in animals after removal of the spleen [4], and consequently there is also more intensive proliferation of these cells. In the bone marrow of rats there were 4.7 times more megakaryocytes on the 5th day after removal of the spleen than in control animals. Thrombocytes were subsequently formed from them. While the number of megakaryocytes constituted 1.7±0.26 in control animals, it was 8.0±0.48 in experimental ones, when scaled to 1000 examined cells. In experimental animals this was associated with 1.5-fold increase in mitotic activity of cells and 3.7-fold increase in number of metaphases with type I structural and functional organization. The increase in number of megakaryocytes and, accordingly, in metaphases with type I structural organization of chromosomes characterize the megakaryocyte hemopoietic class in rats, the distinctive feature of which is that chromosome pairs 18 and 19 are acrocentric, while 20 is metacentric.

It has been proven that there is intensified activity of red bone marrow and increase in reticulocyte precursors of erythrocytes in hypoxic animals and man [2]. In experimental rats, mitotic activity of cells in bone marrow increased by 1.9 times, as compared to control animals and the number of erythroid cells increased by 2.1 times after submitting them to hypoxia for 6 h/day in a pressure chamber at rarefaction corresponding to 9000 m above sea level for 6 days. In this experiment, there was 1.9-fold increase in number of metaphases with type III structural organization (up to 70.0±2.18%). Hence, type III corresponds to the functional and structural organization of chromosomes referable to the erythroid, red class of cells, and it is characterized by the fact that chromosome pairs 18, 19 and 20 are metacentric.

As we know, three hemopoietic precursors--white, red and megakaryocyte--are observed to be formed from the same stem cell in bone marrow [1]. The demonstrated patterns of structural transformation of chromosomes, distinctions of determination of lymphoid, megakaryocyte and erythroid classes of hemopoietic cells in rat bone marrow are of positive importance to more precise identification of processes of chromosome function and hemopoiesis.

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ROLE OF OXYGEN IN RESUSCITATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 26 Feb 85) pp 80-81

[Article by L. A. Bokeriya, N. A. Sokolova and A. S. Konikova (deceased)]

[Text] At the present time, improvement of the system of medical care of cosmonauts is an important problem. For this reason, there are plans for development of a set of resuscitation measures that would be necessary in the case of onset of acute hypoxic and anoxic states, which may occur in sudden emergency situations.

The purpose of the experiment was to examine the mechanism of transition from life to death on the molecular level. Renewal of proteins and nucleic acids, and change in their conformation (spatial arrangement) were used as the main indicators of changes in metabolic processes in case of death due to anoxic anoxia (exsanguination).

With this procedure it was possible to reflect some patterns of biopolymer conversions related to processes of dying and resuscitation. We examined the intensity of synthesis and dissociation of proteins and nucleic acids in the basic organs and tissues of experimental animals: different parts of the brain, myocardium and skeletal muscles, liver, kidneys, lung, spleen, adrenals, thyroid and pancreas, blood, bile and urine.

We submit below the main conclusions drawn as a result of a series of experiments, the results of which were described in detail in several articles [1-4].

1. After onset of the animal's death, elimination of the process of biopolymer renewal was observed, i.e., discontinuation of synthesis and breakdown of proteins and nucleic acids in the organs examined.

2. The process of renewal of biopolymers stopped in all examined organs and tissues, in cellular and subcellular structures 10 min (brain, spleen) to 60 min (pancreas) after onset of death.

3. Perhaps conformational changes in protein molecules related to loss of biocatalytic activity was the cause of cessation of the process of their renewal. These changes can occur due to cessation of delivery of oxygen to the animal's

tissues. Dissociation of biopolymers to structural entities does not occur for several hours afer death.

4. When 10-15 min have elapsed after onset of death, the processes observed at carcass temperature of 36-38°C were virtually irreversible. The resuscitation procedures used at this temperature did not revive the animals.

5. Rapid cooling of the body to 20°C, started 10-15 min after onset of death due to acute anoxia renders reversible the postmortem conformational changes when oxygen is delivered to tissues (by means of perfusion of cooled oxygenated blood), as well as the processes of renewal of biopolymers and restoration of their enzymatic activity long after onset of death (up to 90 min). A few hours after initiating resuscitation measures, there was restoration in the animals of conformation of proteins, metabolism and physiological functions to the former levels.

These studies were the first experimental attempt to demonstrate on the molecular level the origin of changes in different components of a living system in the course of loss and restoration of vital functions. They consisted in essence of postmortem correlations between the nucleoprotein enzyme complex and molecular oxygen. For this reason, when delivering oxygen to the body at this time, its acceptor function is restored, along with metabolism and vital functions. The body temperature shows virtually no change from the baseline. Such reversibility is possible for a short period of time, 10-15 min. Later on, after onset of death, processes of synthesis and breakdown of biopolymers begin to slow down, and there is substantial change in conformation of redox and other enzymes. This is always manifested by drastic decrease in number of reactive sulfhydryl groups of brain and myocardial proteins, which occurs with insignificant body temperature drop. In the case of prolonged absence of delivery of blood into the body, the conformation of protein-enzymes changes, enzymes are inactivated.

Thus, perhaps one of the main stages of inception of living systems is the combination of plastic biopolymer structures with molecular oxygen. This combining must occur constantly and continuously.

When the carcass is saturated with oxygen postmortem, at the time when enzyme conformation has changed and redox processes are arrested, oxygen no longer functions as a triggering factor of vital functions. There is no resuscitation. It can occur only when the conformation of proteins returns to its original appearance. Such correction of the protein-enzyme complex is possible. We succeeded in demonstrating that conformational changes in proteins following death due to acute anoxia may occur differently, and they depend on the body's temperature.

There have been many investigations dealing with the effect of different levels of temperature on protein (in particular enzyme) conformation, which lead to reversible and irreversible loss of catalytic activity in different biological systems.

However, there have been virtually no investigations of the effect of temperature on conformation processes in the organism after death.

Saturation of the body with oxygen, with use of drastic cooling of the animal to 20° after termination of the period of clinical death, again leads to resuscitation. This is virtually impossible in animals that have not been cooled.

Evidently, drastic cooling to 20°C, initiated no later than 10-15 min after death, makes it possible to retain a conformation of proteins-enzymes that enables molecular oxygen to again perform the role of end acceptor of electrons in the respiratory chain for a long time. In this case, resuscitation is possible after a long period of death (up to 90 min).

Probably, in this case the drastic reduction of body temperature plays the leading role in interaction of oxygen with the enzyme complex. The acceptor and conformation functions of oxygen may be manifested in different ways on different temperature levels. Thus, in our experiments, the role of oxygen as a conformation agent could be performed with cooling, whereas its electron-acceptor function during cooling was associated with elevation of the animal's body temperature. Both these functions of oxygen can be manifested at different times, but the conformation function must precede the acceptor function. It is only in this case that oxygen becomes the triggering factor of vital functions.

Separation of these functions of oxygen is demonstrable when the body is in a deep hypothermic state. As a result of lowering body temperature to 20°C, metabolic processes are virtually arrested, and the acceptor function of oxygen is eliminated. As a result, synthesis of macroergic compounds stopped. However, judging by the quantity of reactive sulfhydryl groups of proteins, the original conformation of enzymes was retained at this temperature. Upon subsequent oxygenation of the body with elevation of temperature, there was restoration of the process of electron transfer and vital functions. Such separation into conformation and acceptor functions of oxygen is important to disclosure of the patterns of resuscitation of highly developed biological systems.

Apparently, molecular oxygen plays a multifaceted role in biological phenomena. It participates as a chemical element in building micromolecules and macromolecules, which are elements of the body; it affects conformation of redox enzymes, accepts electrons, thus providing the continuity of their transfer in the chain of energy metabolism, which is essential to vital functions. Reversibility of the transition of a highly developed organism from life to death depends on interaction of molecular oxygen with the protein complex.

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MORPHOMETRIC ANALYSIS OF AORTIC ENDOTHELIUM AND BLOOD SERUM LIPIDS IN HYPOKINETIC RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by A. N. Gansburgskiy and P. P. Potapov]

[Text] On the basis of numerous biochemical investigations, it was concluded [8] that a metabolic background that is beneficial for onset of atherosclerosis develops under conditions of strict limitation of mobility. There are only a few works in the literature dealing with investigation of the condition of the wall of great vessels under hypokinetic conditions [3]. It was stressed [6] that it is necessary to investigate the effect of diminished motor activity on structure of the walls of the great arteries. Such data are needed to determine the extent to which there is a real danger of vascular damage in the case of limited mobility. An effort was made here to characterize the aortic endothelium of hypokinetic rats by means of morphometric methods, and to compare the morphological changes to those in levels of blood serum levels.

Methods

Experiments were performed on white male rats weighing 170-210 g. The animals were placed in individual small cages made of plexiglas. We examined 37 rats (including 7 controls). Experimental animals were sacrificed using ether fumes daily (1 rat at a time) for 1 month. Such organization of the morphological experiment had substantial advantages, since, according to G. S. Katinas [4], arrangement of all cases at the rate of one per point in time with an increasing number of observation times permits more accurate description of dynamics of the process. Control animals were sacrificed on the 4th, 8th, 12th, 16th, 20th, 24th and 28th experimental days. The thoracic aorta was fixed in Bouin's fluid and stained with iron hematoxylin. Mean area of endotheliocytes, their nuclei and cytoplasm, as well as the nucleus-plasma ration, S_n/S_c (lens 90×, ocular 7, binocular attachment 2.5×), were determined by the stereological "field" method [1] using an ocular grid with 27 equidistant points on film preparations of endothelium. Morphometric analysis was performed on 175-200 cells from each animal. In addition, analyzing 8000-10,000 cells in each animal, we counted endothelial cells with karyopyknosis, as well as cells containing 2 nuclei. The dynamics of each parameter were determined by the sliding average method (smoothing for 3 points); reliability of differences was evaluated according to the nonparametric criterion of Wilcoxson-Mann-Whitney

[4]. We used 47 rats (including 24 control animals) for the biochemical tests. The animals were decapitated (5-7 each from the experimental and control groups) on the 7th, 15th, 21st and 30th days of the experiment. We measured cholesterol and phospholipid content of blood serum [2]. The biochemical data were submitted to statistical processing using the criterion of Student and Fisher.

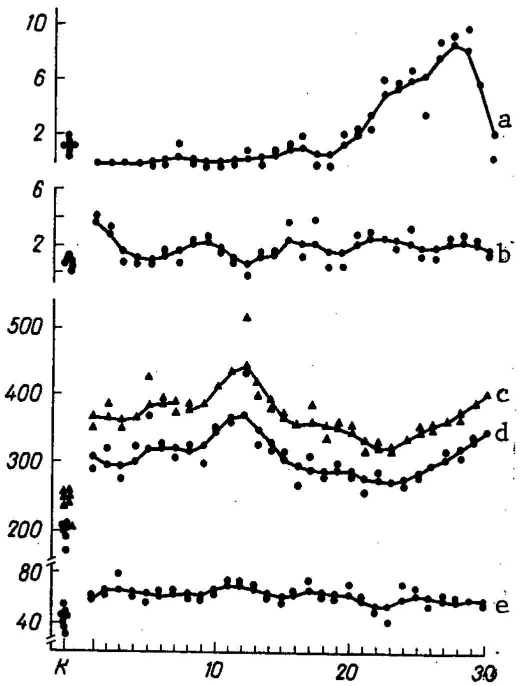

Figure 1.

Dynamics of morphometric parameters of aortic endothelium in hypokinetic rats; x-axis, day of hypokinesia; y-axis, relative number (%) of cellular forms (a, b) and area (in μm^2) (c, d, e)

a) karyopyknosis
b) binuclear cells
c) mean area of cells
d) mean area of cytoplasm
e) mean area of nuclei
K) control

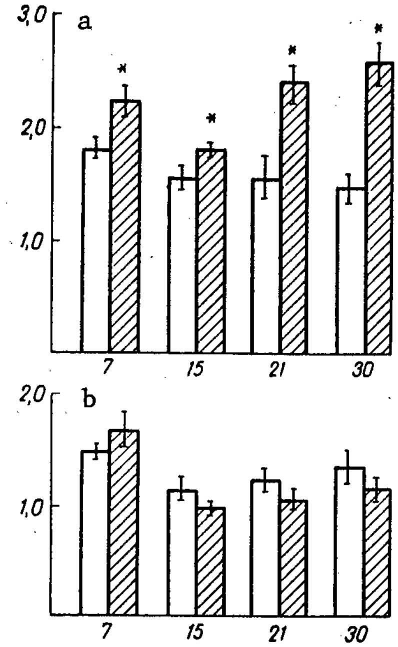

Figure 2.

Cholesterol (a) and phospholipid (b) levels in blood serum of hypokinetic rats; x-axis, day of hypokinesia; y-axis, lipid content (mmol/ℓ); white bars--control, striped--experiment

Asterisk shows statistically reliable changes, as compared to the control (P<0.05)

Results and Discussion

We failed to demonstrate consistent changes in the morphological parameters studied throughout the period of the study in intact animals.

Enlargement of the area of endotheliocytes was found in the 1st week in hypokinetic rats, and this involved both the cytoplasm and nuclei (Figure 1c, d, e). On the first days of the experiment there was also an increase in number of binuclear cells (Figure 1b). No destructive changes were demonstrable. The changes as a whole could be interpreted [7] as a compensatory and adaptive reaction of endothelial cells.

By the end of the 2d week of hypokinesia the percentage of cells with karyopyknosis and two nuclei was close to normal (Figure 1a, b), while the area of nuclei was somewhat increased. The area of endotheliocytes was drastically increased, mainly due to increase in cytoplasm area (see Figure 1c, d). There was appreciably decline of S_n/S_c coefficient, and on the 15th day it constituted 17.7% (versus 23.5±1.2% in the control). The changes were statistically reliable ($P<0.05$).

A significant increase in cytoplasm area was demonstrated on the 21st-30th days of limited mobility. These changes may be indicative of inconsistency between number of endotheliocytes and area on which they are distributed. An adverse finding is that functional activity of nuclei diminished from the 25th to the 30th days of the experiment: maximum decline over the entire period of coefficient S_n/S_c (on the 30th day it constituted 16.6±2.6%; $P<0.05$), and there were noticeable destructive changes in the nuclei; the percentage of pyknotic nuclei reached a maximum on the 27th day of hypokinesia (see Figure 1a). The decrease in number of cells per unit surface, no matter what caused it, in the absence of adequate activation of the nuclear system, can be interpreted as an adverse phenomenon. Under such conditions, increased permeability persists for a long time in areas of damage to the endothelial layer [9]. This ultimately creates favorable conditions for penetration of lipoproteins into the vascular wall [5].

Maximum hypercholesterolemia was demonstrated on the 21st and 30th days of hypokinesia, whereas the phospholipid levels showed a tendency toward decline. As a result, there could be decrease in stability of lipoprotein complexes of plasma. At the same period, we observed substantial impairment of morphology of aortic endothelium. Thus, under the conditions of our experiment, the 21st-30th days of hypokinesia were the most dangerous, from the standpoint of possible damage to vessels. In animals, this period corresponds to the change from the resistance phase to the depletion phase [8]. The demonstrated patterns must be borne in mind when elaborating preventive measures.

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EFFECT OF HYPOKINESIA ON FOOD-PROCURING REFLEXES IN MONKEYS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by V. M. Eliava and T. G. Urmancheyeva]

[Text] Our objective here, related to development of a model of clinostatic hypokinesia (CH) in monkeys, was to test the effects of different forms of restricting motor activity on higher nervous activity of these animals according to parameters of food-procuring skill.

Methods

This study was conducted on 3 Macaca rhesus (Nos 15950, 15953, 15958) males 5-6 years of age. Before the experiment, the monkeys were kept in vivarium cages where they could move freely. We used 3 types of 30-day restriction of movement: small cages (77×77×93 cm), immobilization in primatological chair in vertical position and CH produced by a previously described method [4]. Before starting the experiment, the food-procuring reflex (FPR) in response to an audio signal was developed in the monkeys. The FPR consisted of a successive chain of motor reactions (depressing a lever, running to the feeder 2.5 m away from the lever, etc.). The monkeys ran on moving platforms, which increased the load on locomotion coordinating mechanisms. In each test, we delivered 20 conditioned cues, exposure of which lasted 3 s with 30-s intervals between them. The experiments were started when the monkeys achieved 100% in FPR performance. We determined the latency period of the reflex (LP; from the start of exposure of signal to depressiosn of lever) and motor reaction time (MRT; from time of depression of lever to opening of feeder). In all cases, the experiments lasted 30 days. FPR testing was performed on the 10th, 20th and 30th days, as well as 5th, 11th and 15th days after submitting the animals to CH.

Results and Discussion

Keeping the monkeys in small cages had no effect on the level of FPR (Figure 1A). At the same time, there were sporadic changes at some stages of hypokinesia in time parameters of this reflex. Long-term immobilization in primatological chairs also failed to affect the level of performance of the FPR chain (Figure 1B). The observed changes in LP and MRT were in different directions and unstable.

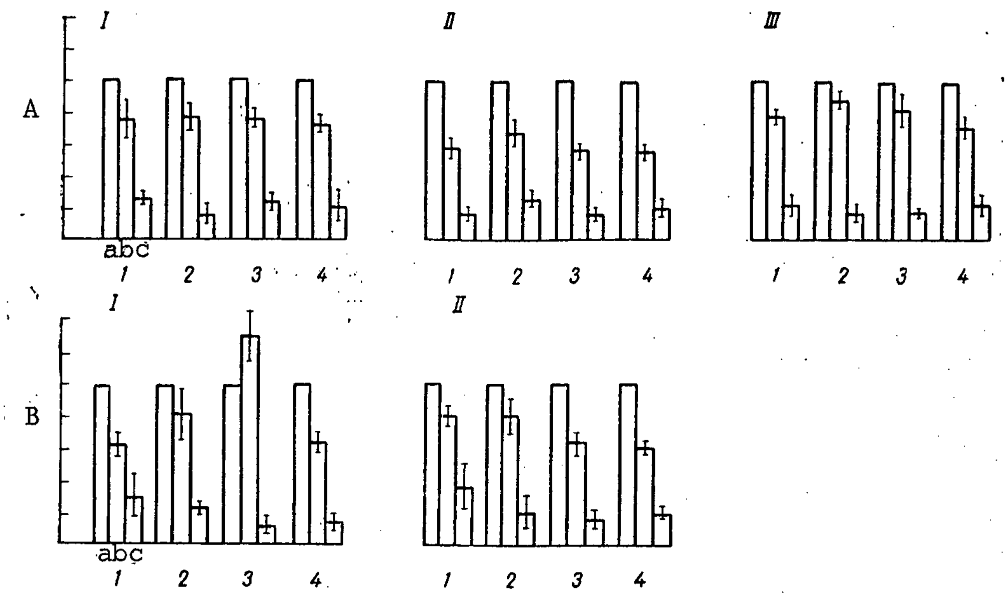

Figure 1. Effect on characteristics of food-procuring reflex of restriction of motor activity of monkeys in small cage (A) and primatological chair (B)

Here and in Figure 2:
- I) monkey No 15950
- II) monkey No 15958
- III) monkey No 15953
- a) level of FPR (%)
- b) motor reaction time (s)
- c) latency periods of FPR (s)
- 1) baseline period
- 2,3,4) 10, 20 and 30 days, respectively, of restricted motor activity

Submitting monkeys to CH led to significant changes in both level of performance of the tested chain of reflexes (to the extent of complete absence of responses to signals) and time parameters. When the conditioned cue was turned on, the monkeys manifested general restlessness, scratched themselves and responded to some cues by performing the first component of the FPR, depressing the lever. In most cases, LP was increased. It is only in isolated cases that monkeys Nos 15950 and 15953 performed the entire chain of motor actions upon delivery of the conditioned signal (Figure 2, I and III). In this case, LP and MRT were significantly longer than in the baseline period. When testing FPR of monkey No 15958, it did not respond adequately to one of the conditioned signals at all stages of the study (Figure 2, II).

In the recovery period, there was gradual restoration of motor activity and FPR performance. On the 5th day of the recovery period, monkey No 15950 presented maximum activity (Figure 2, *1* and *5*), and it performed the entire FPR chain in 50% of the cases. LP was close to the baseline. MTR remained almost twice as long. On the 11th day of the recovery period, the responses of monkeys No 15950 and 15953 reached 70%, while the time parameters exceeded the baseline, particularly MRT (Figure 2, I, II, *6*). On the 15th day, a 70% performance of FPR was also demonstrated in monkey No 15958. Level of FPR was 75% in monkey No 15958, while LP and MRT were within the baseline range.

In monkey No 15950, reflex performance was at 100% on the 15th day of the recovery period, LP was close to baseline values, while MRT remained longer (4.46±0.17 s, versus 3.42±0.11 s in the first tests).

Thus, analysis of experimental data shows that keeping monkeys immobilized in horizontal position leads not only to disturbances in the motor system, which are manifested primarily by increase in time of performance of motor skills with unrestricted movement, but also to a disorder in conditioned reflex activity. The fact that there were some cases of depression of the lever by the animals, intersignal approaches to and action on the feeder, as well as adequate reponses to a natural stimulus (bait near feeder), indicated that food motivation was retained, and it was possible to perform purposeful movements, although there were some coordination disturbances. In the recovery period, in the presence of normalization of general motor activity, there was gradual restoration (without special training) of both the level of FPR and time parameters--LP and MRT.

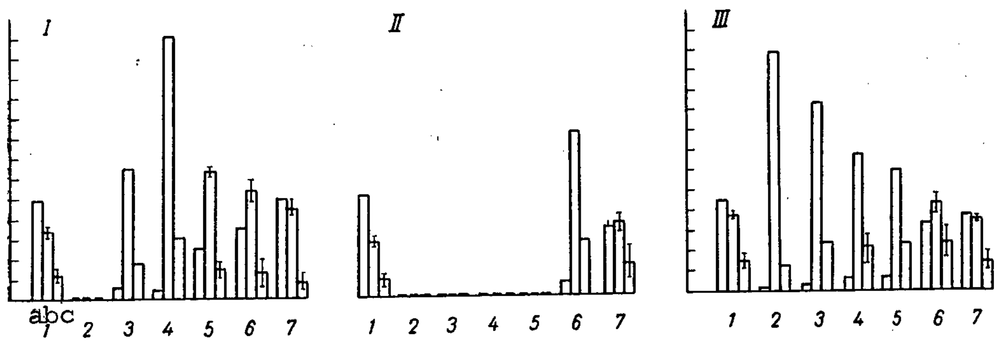

Figure 2. Effect of submitting monkeys to CH on characteristics of performance of food-procuring reflex

1) baseline period
2, 3, 4) 10, 20 and 30 days, respectively, of CH
5, 6, 7) 6th, 11th and 15th days, respectively, of recovery period

The results, which indicate that submitting monkeys to CH leads to significant disturbances of coordination, are consistent with those described previously [4]. At the same time, we obtained here a quantitative evaluation of changes in some characteristics of locomotor acts. The profound disturbances in conditioned reflex activity demonstrated in monkeys are consistent, to some extent, with the data of L. N. Khruleva [5], who described considerable changes in higher nervous activity due to hypokinesia in white rats lasting up to 30 days. According to A. A. Dzhokua [3], long-term CH had no appreciable effect on the level of performance by Macaca rhesus monkeys of a motor test, whereas the characteristics of the motor act were subject to significant changes [2]. However, in that investigation, the monkeys were trained to perform motor acts in primatological chairs. During the tests, the working foot of the animal remained always in the original position on the actograph pedal. In our experiments, however, the monekys had to perform a chain of motor acts, including displacement in space, in response to a conditional cue.

Apparently, the emotional tension that developed and changes in afferent flow led to significant depression of functional state of the central nervous system. It can be assumed that as a consequence there were considerable disturbances in mechanisms of organization of adequate reaction to cues with alimentary significance. The negative emotional reaction (fear), which usually developed in monkeys when coordination was impaired, also played a substantial part [1].

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PARAMETERS OF CARBOHYDRATE AND LIPID METABOLISM IN RATS IN RECOVERY PERIOD FOLLOWING 30-DAY HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 30 Nov 84) pp 85-87

[Article by P. P. Potapov and N. A. Tikhomirova]

[Text] It is of considerable interest to investigate metabolism in the period of recovery following restriction of mobility differing in duration, in order to determine the patterns of recovery and elaborate optimum rehabilitation measures [7]. We report here on a study of lipid and carbohydrate levels in rat liver and blood serum at different stages of the recovery period following 30-day hypokinesia.

Methods

Experiments were performed on 66 white male rats initially weighing 165-190 g. The animals were put in tight individual chambers made of plexiglas. The animals were switched to group cages after 30-day immobilization. Control rats were kept in ordinary vivarium cages for all of this time. Animals were decapitated on the 30th day of hypokinesia and on the 7th, 15th, 21st, 30th and 60th days of the recovery period. Control animals were decapitated and examined at the same times as experimental ones. The parameters in question remained constant throughout the period of the investigation in intact animals, so that the results of analysis made on these rats were combined in the same group. We analyzed blood serum and liver tissue. Total lipids (TL), cholesterol (CS) and phospholipids (PL) were assayed by the methods described in the manual by A. A. Pokrovskiy [2]. Triglycerides (TG) were assayed by the method of Stolz et al. [12], free fatty acids (FFA) in serum by the method of Duncombe [9], and blood sugar by the o-toluidine method. Liver glycogen (GG) was assayed [10, 11].

Results and Discussion

Moderate hypoglycemia, hypercholesterolemia and elevation of FFA levels in blood were demonstrated on the 30th day of hypokinesia (Tables 1 and 2). In the liver, there was an increase in TL, TG and CS content. Conversely, GG level dropped significantly. These findings are similar to results previously obtained on the same model of hypokinesia [5, 7]. One week after hypokinesia, we observed considerable changes in most biochemical parameters. Blood sugar was noticeably

higher than normal; we also demonstrated hypertriglyceridemia and hypocholesterolemia, while FFA levels in serum dropped. In the liver, lipid content diminished, while GG was already almost 2.5 times above normal and almost 10 times higher than on the 30th day of hypokinesia. Noticeable hyperglycemia and low FFA levels persisted to the end of the experiment. Serum PL dropped on the 30th day of the recovery period, but was normal at other tested times. TG content did not differ appreciably from the control starting on the 15th day of the recovery period. Hypercholesterolemia was demonstrable on the 21st and 60th days of the recovery period. GG level was above normal in hepatic tissue up to the 60th day of the recovery period, TL and TG levels remained low for a long time. Increase in CS content of the liver was found 1 month after hypokinesia.

Table 1. Blood sugar and serum lipid levels in rats in recovery period following 30-day hypokinesia

Parameter	Control rats	30-Day hypokin.	Recovery period, day				
			7	15	21	30	60
Sugar, mmol/ℓ	4,80±0,08 (25)	4,49±0,08* (5)	6,25±0,23* (6)	5,33±0,12* (6)	5,78±0,12* (7)	5,62±0,22* (6)	5,28±0,08* (6)
TL, g/ℓ	2,93±0,06 (22)	3,16±0,13 (5)	3,25±0,13* (7)	2,62±0,05* (6)	3,10±0,10 (6)	2,73±0,13 (7)	2,75±0,11 (6)
TG, mmol/ℓ	1,37±0,02 (24)	1,27±0,12 (5)	1,64±0,04* (7)	1,28±0,06 (7)	1,41±0,06 (7)	1,28±0,05 (7)	1,35±0,03 (6)
CS, mmol/ℓ	1,70±0,04 (27)	2,55±0,14* (5)	1,48±0,09* (7)	1,61±0,11 (7)	1,94±0,08* (6)	1,88±0,09 (7)	2,05±0,12* (6)
PL, mmol/ℓ	1,20±0,03 (22)	1,16±0,08 (5)	1,37±0,12 (7)	1,11±0,08 (7)	1,16±0,06 (7)	1,01±0,07* (7)	1,08±0,07 (6)
FFA, μequiv/ℓ	458±15 (21)	553±19* (5)	324±28* (7)	371±25* (7)	—	397±20* (7)	392±24* (6)

Note: Here and in Table 2, number of animals given in parentheses; asterisk indicates statistically reliable changes as compared to the control (P<0.05).

Table 2. Glycogen and lipid content of rat liver in recovery period following 30-day hypokinesia

Parameter	Control rats	30-Day hypokin.	Recovery period, day				
			7	15	21	30	60
GG, g%	4,23±0,21 (27)	1,01±0,28* (5)	10,09±0,68* (6)	5,39±0,42* (6)	5,78±0,68* (7)	5,73±0,45* (7)	6,62±0,96* (5)
TL, g%	5,58±0,11 (18)	6,77±0,09* (5)	4,15±0,06* (5)	5,00±0,20* (5)	4,23±0,14* (7)	3,87±0,12* (6)	4,36±0,19* (6)
TG, μmol/g	22,5±0,6 (18)	29,5±1,6* (5)	17,1±1,2* (5)	18,6±1,0* (5)	17,8±1,0* (7)	16,4±0,6* (5)	17,1±1,6* (6)
CS, μmol/ℓ	6,97±0,16 (18)	8,91±0,57* (5)	4,92±0,21* (5)	7,12±0,34 (5)	7,23±0,28 (7)	8,70±0,31* (5)	6,45±0,23 (6)

We were impressed by the fact that most changes on the 7th day of the recovery period were in the opposite direction from those observed during hypokinesia, and those referable to TL, TG and GG content of the liver were quite persistent.

Overly restoration of some parameters had also been reported previously in the recovery period following 7-, 15- and 90-day hypokinesia [4, 6, 8]. Apparently these changes are universal and inherent in metabolic recovery processes after hypokinesia whatever its duration may be. There was particularly marked accumulation of GG in the liver following 30 days of restricted mobility. Apparently, in this case processes of carbohydrate synthesis prevailed significantly over processes of their breakdown. It is logical to assume that a 10-fold (as compared to 30th day of hypokinesia) increase in polysaccharide content of the liver can occur only if there is considerable intensification of gluconeogenesis and glycogen synthesis. The noticeable hyperglycemia indicates that processes of mobilization of carbohydrates from the liver were not impaired. It can also be noted that the mechanisms responsible for maintaining normal correlations between blood sugar and FFA were not impaired throughout the period of the experiment. The data available at this time do not give us grounds to interpret the demonstrated changes in carbohydrate metabolism as being pathological. However, a definitive conclusion can be drawn only after investigation of processes of carbohydrate breakdown in tissues, particularly muscle tissue.

Intensification of gluconeogenesis could limit TG synthesis [1]. This could be one of the causes of decline of their level in the liver in the recovery period. A shortage of fatty acids could play some part in lowering TG synthesis. Their synthesis is apparently depressed in the recovery period due to decrease in citrate content of the liver [3], which is an activator of fatty acid synthesis [1].

Still unclear are the causes of the significant changes in cholesterol levels in the liver and blood serum. The marked tendency toward accumulation of cholesterol at the late recovery stages can be viewed as an adverse phenomenon.

The findings indicate that the time of normalization of metabolism can be considerably longer than the duration of preceding hypokinesia. Further investigations are needed to assess the effect of the demonstrated biochemical changes on recovery of body functions, particularly functional recovery of the cardiovascular and muscular systems. To do this, it is necessary, first of all, to determine the possibility of using different substrates in energy metabolism.

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PROTECTIVE ROLE OF ENDOGENOUS MORPHINE-LIKE SUBSTANCES IN MICE WITH ACUTE HYPOXIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 27 Mar 85) pp 87-88

[Article by V. V. Yasnetsov, V. V. Chukayev, S. K. Karsanova and V. L. Popkov]

[Text] We previously demonstrated that naloxone, which is a specific antagonist of opiates and opioids, shortens the life of mice contained in a pressure chamber [1] (model of normobaric hypoxic hypoxia--[2]). On the basis of these data, the hypothesis was expounded that endogenous morphine-like agents may play a protective role against acute hypoxia, expressing their antihypoxic action through opiate receptors. To continue the above investigations, we decided to obtain new evidence of this thesis with use of another model of hypoxic hypoxia. In addition to naloxone ("pure" antagonist), we used here nalorphine (agonist-antagonist), and we compared the effects of specific opiate antagonists to the effect of narcotic analgesics--morphine ("pure" agonist of opiate receptors) and pentazocine (which has mild antagonistic properties).

Methods

Experiments were performed on mongrel whie male mice weighing 18-26 g. We simulated hypobaric hypoxic hypoxia in mice by placing them in a pressure chamber and "elevating" them to "altitudes" of 10,500-10,700 m at the rate of 30 m/s [2]. We recorded their survival time (until respiration stopped) under conditions of hypoxic hypoxia. All agents were given intraperitoneally in a volume of 0.05 mℓ/10 g body weight. Naloxone was injected 5-10 min before putting the mice in the chamber and the other agents, 15-20 min before this. Isotonic solution of sodium chloride was injected to the control group of animals.

Results and Discussion

Data concerning the effect of the agents on survival time of mice submitted to hypobaric hypoxia are listed in the Table. It shows that, in a dosage of 10 mg/kg, morphine enhances resistance to hypoxic hypoxia. This is also known from the literature [2]. Pentazocine in a dosage of 25 mg/kg has an effect that is analogous to morphine. With use of low doses of pentazocine (1 and

10 mg/kg, there is a tendency toward shortening of mouse life expectancy, which can apparently be related to this agent's antagonistic properties.

Effect of different agents on mouse resistance to hypobaric hypoxic hypoxia

Agent		Total number of mice	Overall survival time, s (M±m)	Deaths in "ascent"	Survival at "high altitude," s (M±M)
Morphine (10)		56	146±20*	4	158±20*
	Control	56	91±13	7	104±14
Pentazocine (1)		53	58±5	1	60±5
	"	48	65±7	1	66±7
Pentazocine (10)		45	49±8	6	56±9
	"	45	72±9	4	79±9
Pentazocine (25)		65	104±18***	5	112±19***
	"	65	46±5	7	51±5
Nalorphine (1)		37	29±5****	8	37±5***
	"	29	67±9	0	67±9
Nalorphine (5)		48	68±9	3	72±9
	"	42	83±8	1	85±8
Nalorphine (10)		48	88±7	1	90±7
	"	41	102±12	1	104±12
Naloxone (0.1)		82	111±20	15	136±23
	"	80	145±26	7	158±28
Naloxone (1)		69	104±21**	10	122±24*
	"	64	199±30	2	206±31
Naloxone (10)		44	44±7***	11	58±8***
	"	37	184±46	2	195±48

*P<0.05, **P<0.02, ***P<0.01, ****P<0.001, as compared to control (Student's criterion)

Note: Dosage is indicated in parentheses (in mg/kg). Life expectancy of mice that died during "ascent" to "high altitude" is taken as 0.

Unlike narcotic analgesics, their antagonists--naloxone and nalorphine--shorten the life of hypoxic animals. Thus, naloxone reduces mouse resistance to acute hypoxic hypoxia. Not only is survival time at "high altitude" reduced, there is also an increase in deaths during the "ascent," as compared to control animals. For example, in groups given naloxone in doses of 1 and 10 mg/kg, 21 mice died during the "ascent" versus 4 animals in control groups. In a dosage of 1 mg/kg, nalorphine has action that is similar to naloxone in the same dosage. However, when dosage is increased to 5-10 mg/kg, this effect is canceled out, and there is only a tendency toward shortening of survival time of hypoxic animals. This can be attributed to the fact that with increase in dose of nalorphine, which is an agonist-antagonist of narcotic analgesics, it begins to present morphine-like properties.

Thus, these studies revealed that use of low doses of naloxone or nalorphine to block opiate receptors diminishes mouse resistance to hypobaric hypoxic hypoxia. This may indicate that endogenous morphine-like substances (enkephalins, endorphins, etc.) play a protective role in animals with acute hypoxia.

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DISCUSSIONS

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DYNAMICS OF BIOELECTRIC ACTIVITY OF HUMAN BRAIN IN A CONTINUOUS WAKING STATE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 30 Aug 84) pp 88-91

[Article by V. P. Tychina and A. P. Nechayev]

[English abstract from source] Electroencephalographic parameters can be used to detect early signs of fatigue which is of practical importance. Experiments were carried out on three healthy men to identify a limited number of symptoms allowing a rapid evaluation of operator's work capacity. The subjects were kept in long-term isolation. The study revealed general trends and individual variations in brain bioelectrical activities that reflected their performance during a continuous work with natural sleep deprived for three days.

[Text] Electroencephalography, which is an objective method of monitoring bioelectric activity of the human brain, still does not have an unambiguous interpretation of many of its elements. Apparently, one of the causes is the integral nature of the electroencephalographic curve recorded from many neuronal units of the brain [1, 5, 8, 11-13]. At the same time, many researchers indicate the presence of zonal distinctions of bioelectric activity due to the morphological and functional structure of the cerebral hemispheres. Dynamic spatial associations are formed when the waking brain is in different states, and they are associated with specific functional reactions [5, 6, 8, 11]. There are also differences in interpretation of electroencephalograms (EEG) when assessing work capacity and signs of fatigue. A number of investigators have stressed the fact that sleep phases can be compared to signs of fatigue [2, 3, 7, 10].

It is of practical interest to define the range of EEG characteristics corresponding to manifestation of early signs of fatigue. Our objective here was to search for a limited set of criteria for rapid evaluation of operator work capacity. We tried to determine, on the basis of analysis of the EEG, the limits of fatigue developing in the course of 3 days of continuous work (CW).

Methods

The studies were conducted with the participation of 3 healthy subjects (S-1, S-2, S-3) 30 to 50 years of age, who were isolated for 3 months and performed

a program of operator work. After completion of the period of their adaptation to these conditions, we made a 3-day study of CW ("insomnia"). EEG from the occipital leads was recorded twice a day during CW, at 1000 and 1700 hours. In the morning, the EEG was recorded during performance of operator work, which consisted of compensatory tracking of a random signal. In the evening, it was recorded during work using psychological form methods. Before starting each type of activity and after it, we recorded the "baseline" in a relaxed position. EEG recording was continued until the subjects presented distinct signs of onset of sleep. When assessing the degree of lability of excitatory and inhibitory processes in the brain, we took into consideration the nature of verbal activity, quality of performance of elementary arithmetic operations and, occasionally, accuracy in working with a coordinograph. No stimulation tests were performed. Concurrently with the EEG, we recorded the electrocardiogram (ECG), electromyogram, respiration rate, heart rate, and we visually monitored operator performance. S-1 and S-2 completed the entire CW program. However, analysis of the EEG of S-2 in the afternoon of the 3d day was incomplete, due to artefacts caused by technical flaws of recording. In S-3, the EEG was taken on the 1st and 2d days of CW and in the period of morning operator work on the 3d day, after which he was told to rest and sleep in accordance with the protocol of the experiment. The final EEG was taken on S-3 after he rested, in the afternoon of the 4th day.

Results and Discussion

Observations revealed that the subjects retained a rather high level of work capacity throughout the CW period. However, analysis of the EEG enabled us to detect some general tendencies and individual distinctions in the dynamics of bioelectric activity of the brain. Thus, already in the afternoon of the 1st day of CW, we observed dominance of slow synchronized waves. Fast waves, on the contrary, were diminished, with concurrent increase in their amplitude. On the 2d and 3d days, slow rhythms were more distinct, both during performance of assignments and periods of relaxation. Bioelectric activity of the brain showed obvious prevalence of slow waves immediately after the order to relax.

There was more distinct regression of fast waves with concurrent decrease in their amplitude and appearance of synchronized slow waves in S-1 and S-2. Such changes in basic rhythm of EEG were the least marked in S-3. The parameters of EEG rhythms in S-3 were virtually identical on all mornings of CW and in the afternoon of the 4th day (after sleeping).

In S-2, bioelectric activity was intermediate, but quite similar to the EEG of S-1. It should be added that S-2 presented a distinct individual feature: already on the 1st day of CW, there were isolated complexes of the peak-wave type on the EEG, and the frequency of their appearance subsequently had a tendency toward increasing. However, we did not notice synchronization of these complexes. In the course of making the recording, we were able to observe distinctive acceleration of fast waves after manifestation of such a complex. The latter can apparently be attributed to the mechanism of endogenous stimulation of bioelectric activity of the brain. Development of fatigue was associated not only with changes in bioelectric activity of the brain, but appearance (particularly by the end of the 3d day of CW) of mild athetosis, tonic spasm

of small hand muscles (in S-1), diminished communicability, withdrawal (S-2). These signs were seen in the subjects after CW also, along with mild ataxia and the subjective feeling of fatigue toward the end of the experiment.

In order to perform ongoing analysis of bioelectric activity, we grouped EEG elements with consideration of the known classifications of waking and sleep states in healthy adults [2, 5, 6, 8-13]. This enabled us to single out three types of EEG features comparable to different states of work capacity, which were arbitrarily designated as follows: work level (WL), low tonus of cerebral structures (LTCS) and sleep level (SL).

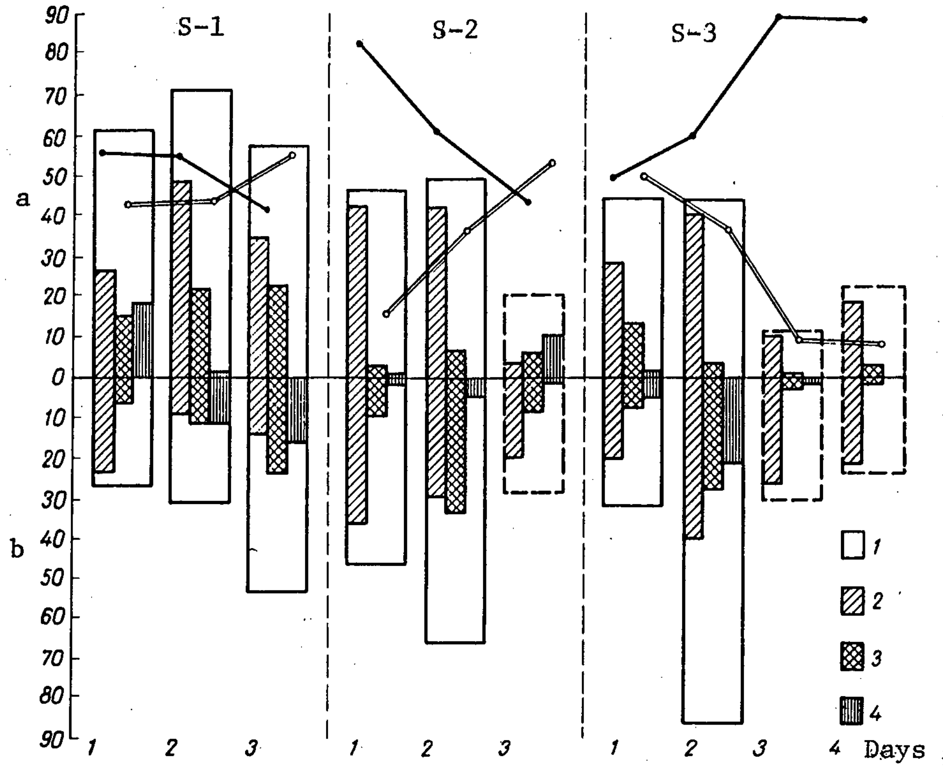
WL of cerebral hemispheres corresponds to the classification group of active wakefulness. Here, there is dominance of low-amplitude fast rhythms with manifestation of β and α waves, indicative of activation of cerebral structures during periods of active work. This coincided with the individual working state of each subject, provided he had sufficiently active reactions to the investigators commands.

LTCS corresponds to a broad classification spectrum, in which there is build-up of synchronized, high-amplitude slow rhythms with groups of α waves. Outwardly, this state was characterized by relaxed wakefulness bordering on drowsiness (superficial and moderate sleep). In response to the order to relax, the subjects showed an increased desire to assume a position of overall relaxation. Some inhibition of motor and verbal reactions was particularly manifest in the afternoon during recording of baseline values.

SL corresponds to stages III and IV in the classification of sleep. Here, we observed further increase in synchronization of slow, high-amplitude rhythms, definitive replacement of fast waves by ν and δ waves, less frequent appearance of sleep spindles. In some cases, the decrease in amplitude of synchronized slow waves led to flattening of the curves. In this period, all subjects presented inhibition, drowsiness with signs of relaxation, sleep, twitching in their sleep, rapid awakening after these signs followed by onset of sleep.

Use of these parameters of brain activity enabled us to demonstrate some patterns in dynamics of work capacity. The level of work activity of the brain remained rather high in all subjects during operator work of tracking, and this apparently caused them to have high motivation to perform the task. Levels of diminished tonus of cerebral structures, to the extent of onset of sleep level, were manifested during work with the forms, as well as when recording baseline tracings. Visually, this coincided with signs of drowsiness and sleep.

With reference to frequency of different factors in this study, it must be noted that working activity of the brain in S-1 and S-2 diminished during "insomnia," after which it became low (see Figure). Thus, the percentile parameters on the 2d day were as follows: WL 55.8 and 62.1%, LTCS + SL 44.2 and 37.9% in S-1 and S-2, respectively. The points of intersection on the graphs characterize the moment of decline of WL and start of dominance of the sum of LTCS and SL on the 3d day of CW. On these days, we observed similar percentages for levels of brain activity in both subjects (WL constituted 44.1 and 46.9%, while the sum of LTCS and SL was 55.9 and 53.1% in S-1 and S-2, respectively.



Time and percentage of levels of bioelectric activity of the brain. X-axis, days of CW; y-axis: a) working time (min), b) time of baseline recording (min); 1) zone of EEG tracing (min), 2, 3, 4) duration of WL, LTCS and SL, respectively (in min). The single line indicates dynamics of WL (%), and the double line, the same for LTCS + SL (%); dash line refers to results of partial analysis

We cannot rule out the possibility that this circumstance indicates that there is some similarity of neurodynamic processes that develop in the brain under the effect of fatigue, and that there is "evening out" of its bioelectric characteristics, regardless of a person's individual distinctions. It is known that, in the presence of long-acting factors that elicit fatigue, the changes in bioelectric activity in the cerebral hemispheres are characterized by unstable desynchronization of the basic rhythm followed by change to synchronized slow waves.

At this time, there is prevalence in subcortical centers of high-amplitude slow waves, among which there are occasional groups of high-frequency waves. When such factors are present for a long time, alternation of desynchronization and hypersynchronization phases could be replaced by noticeable decrease in bioelectric activity of the brain, which is associated with such reflex disorders as athetosis, seizures, respiratory disorders and others [2, 4, 7].

By considering data in the literature and our findings, we can conceive of the mechanism of fatigue as a process of gradual development of inhibitory

phenomena in successive levels of the brain. At first, they develop in cortical structures as the philogenetically more recent elements, which are the most sensitive to different factors, and it is characterized by such signs as relaxation, confused consciousness, sleepiness, etc. After the receptor zones, fatigue extends to associative and then subcortical centers. As we know, the stem level, including the rubrospinal pathway, is the last to be "exhausted," and this was noted in our investigation in the form of appearance of mild signs of athetosis and ataxia.

Thus, the continuous work mode was found to be a rather potent factor influencing the brain's energy balance. Use of the arbitrary parameters of brain activity that we introduced made it possible to demonstrate the qualitative features of its neurodynamics attributable to individual distinctions of the central nervous system.

Analysis of our data enabled us to offer one possible explanation of the mechanism of development of fatigue, which is based on the assumption that individual adaptive reactions are replaced by certain "unified" neurodynamic processes of a general nature.

This was an exploratory investigation. For this reason, in order to improve the reliability of the results, it is necessary to further investigate the potential of the approach we have described in model experiments together with dynamic monitoring of neurological status and other psychophysiological methods.

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NEW BOOK DEALS WITH SPATIAL ORIENTATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Review by A. A. Gyurdzhian and Yu. Yu. Shipkov of book "Spatial Orientation (Theory, Experiments, Application), edited by H. L. Pick and L. P. Acredolo, New York--London, Plenum Publishing Corporation, 1983, 378 pages]

[Text] This collection is compiled on the basis of the proceedings of a conference on spatial orientation (SO) and spatial perception, which convened at the University of Minnesota on 14-16 July 1980. The book consists of the following 5 sections: 1) Comparative physiological, comparative psychological and age-related aspects of SO; 2) SO in some groups of people (the mentally retarded and elderly); 3) ability to use maps and mechanisms of cognition of space; 4) language and cognition of space; 5) cognition of space and processing of information about space.

In the article by N. L. Hazen (University of Texas), there is discussion of the mechanisms and distinctions of SO in different representatives of the animal kingdom as related to ecological conditions and ethological factors, development of ability for SO in the course of individual life, homologous and analogous mechanisms of SO in different animals. In the conclusion of this article, the author discusses the comparative distinctions of SO and conceptions of space in different races and peoples, as related to climatic and geographic conditions, and life style.

The author of the second article, J. J. Rieser (Department of Psychology and Human Development at Vanderbilt University in Nashville, Tennessee), discusses the very interesting question of how SO and a "conception" of mutual location of different segments of a maze are formed in experimental animals on the basis of their first inspection of different places in a maze and segments of paths between these places. This enables them to extrapolate their experience and find the shortest path between points, which they had not used before. At the end of the article, the author submits results of analogous studies conducted on children of different ages and on young people.

In the brief final article of this section, one of the editors of the book, H. L. Pick (Institute of Child Development, University of Minnesota), sums up the data of the two above-described articles, as well as other works in this direction.

The first article of the second section of this collection is by R. G. Golledge, G. D. Richardson (both from the Geography Department of the University of California at Santa Barbara), J. Rayner and J. Parnicky (Ohio State University), and it deals with the representation of locality and immediate spatial environment in the minds of mentally retarded people. This representation (cognitive map) undergoes certain formative stages as people become acquainted with their spatial environment. The authors maintain that such formation does not reach the highest stages, which are inherent in cognitive maps of healthy people, in the mentally retarded. As a result, their maps are one-dimensional rather than two-dimensional. Extensive experimental material is submitted in this paper.

The next article in this section, written by R. Ohta (Department of Psychology, University of West Virginia), deals with the question of SO in old age. In his survey, the author shows that there is considerable deterioration in old age of such characteristics of mental functions as absolute threshold of perception, color discrimination, gaging depth, ability to integrate specific components of the environment, memory for the shape of objects, etc. He also submits the results of a study of the quality of representation of the environment in the human mind, which indicate that worsening of parameters in old age is due to poorer memory, rather than diminished capacity for integration of spatial information. The author remarks that, along with deterioration of SO, with age there is development of certain compensatory mechanisms for solving spatial problem situations.

E. Foulke (University of Louisville, Kentucky) discusses a special applied problem, the independent movement of the blind. He discusses criteria that determine the success of such movement: independence (i.e., complete independence), safety, convenience, pleasure, efficiency (speed, accuracy) and expediency. Special training programs have been elaborated to provide for effective independent movement of patients. The author assesses their use and observes that these programs are not effective enough, since they do not provide answers to questions of how and in what form information should be presented to a blind individual. In his opinion, a general theory must be expounded, which would be based on human perceptive and cognitive capacities, in order to answer these questions.

The last article in this section was written by L. P. Acredolo (Psychology Department, University of California at Davis), co-editor of this collection; he sums up the data in this section, as well as results of other studies on the problem of SO in special groups of people. In particular, he discusses factors that cause difficulties in SO for some groups: those with atypical visual input, neurological distinctions, distinctions referable to passive movement in space and its limited size, distortion of spatial information.

In the third section of the collection, Z. M. Simutis and H. F. Barsam (Research Institute for the Behavioral and Social Sciences, U. S. Army) discuss another problem of applied psychology: assistance to soldiers in visualizing a locality on the basis of a presented map. They assume that there are three ways of overcoming difficulties in reading maps: screening people to read maps on the basis of their individual psychological characteristics in perception of space, improving methods of making maps and training people to read them. The article provides an analysis of studies that have already

been carried out that are viewed as the start of work on a problem that is still far from being solved.

In the second article of this section, P. W. Thorndyke and S. E. Goldin (Rand Corporation) discuss the results of their investigation (which was requested by the Research Institute for the Behavioral and Social Sciences, U. S. Army) of mechanisms of spatial skills and conceptions. Since these mechanisms are based on capacities people have and specific teaching methods, they analyzed the influence of these factors. The authors arrive at the following conclusions: during training, information about space must be selected on the basis of the requirements for a specific task; if there are difficulties in accessing the real environment as a source of information, one should use imaginary movement in a locality by means of screening a special film; in defining the tasks put to military personnel, one should bear in mind individual differences in space perception; use of various training strategies is recommended, depending on the specifics of the task and individual capabilities.

This section concludes with a survey by H. L. Pick and J. J. Lockman (Tulane University, New Orleans, Louisiana) of the principal problems of map reading and individual differences in this process.

The fourth section deals with the expression of space in language. It begins with an article by L. Talmy (University of California at Berkeley). On the example of the English language, he shows how spatial, geometric and figurative background relations are conveyed by linguistics, and how words and diagrams contained in the frame of a sentence serve to conceptualize and formulate spatial information. L. Talmy observes that, on the microstructural level of language, its important features is its schematic nature, and he examines the basic properties of schemes of spatial definitions (idealization, abstraction, topology), as well as correlations between these schemes.

W. Klein (Max Planck Institute of Psycholinguistics, Holland) discusses the use in language of expressions that define the spatial relations mentioned by the speaker. Following in the footsteps of K. Buhler, the author refers to such definitions as deictic. He singles out and analyzes in detail the elements of spatial definitions, in particular, the spatial position of the speaker, a number of implicit reference points, principles for limiting the space in question, etc. In the concluding part of the article, there is discussion of the question of the speaker's conception of itinerary in a locality and distinctions of similar conceptions in children.

The well-known linguist, Ch. J. Fillmore, Department of Linguistics, University of California at Berkeley) analyzes the articles by L. Talmy and W. Klein in the last article [of this section].

In the last section of this collection, J. C. Baird and M. Wagner (Dartmouth College, New Hampshire) offer an original model of mental representation of spatial characteristics of the environment in the form of cognitive maps. They believe that cognitive maps are formed in the mind on the basis of a set of distances between different points in the environment taken in pairs. In the opinion of the authors, the place for spatial elements on a cognitive map is found by means of their detailed description of the procedure for finding the third vertex of a triangle.

B. Kuipers (Psychology Department, Tuft University) explores in his article the question of guidelines and forms of structuring and designing cognitive maps.

This section and the collection as a whole ends with the brief survey by F. Attneave (Psychology Department, Oregon State University), in which he expresses his views on the psychological nature of cognitive maps.

Unfortunately, this collection which pursued the goal of submitting to the reader an analysis of human and animal spatial behavior in their natural environment, as well as under meticulously controlled experimental conditions, and to acquaint him with data referable to a wide range of disciplines, covered only the views of proponents of cognitive psychology. The book does not include investigations and conceptions of physiologists on the question of SO, in particular, the views of I. S. Beritashvili and other Soviet scientists which have gained worldwide recognition, as well as the knowhow acquired in the field of aviation and space medicine.

This collection is of definite interest to a wide circle of psychologists, neuropsychologists, physiologists and specialists in aerospace medicine.

CURRENT EVENTS AND INFORMATION

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COMPARISON OF STRUCTURE OF BIBLIOGRAPHIC REFERENCES USED BY CONTRIBUTORS TO THE PERIODICALS, KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA AND AVIATION, SPACE AND ENVIRONMENTAL MEDICINE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (manuscript received 25 Jan 85) pp 93-95

[Article by S. A. Rozhkov and S. G. Kara-Murza]

[Text] Acceleration of development of science has caused increased interest in studying the structure of scientific directions and evaluating research being done. As a rule, a specialized scientific periodical serves as the center for scientific communication between researchers working in the same field. One of the possible approaches to this problem is based on analysis of bibliographic references [1-3]. When authors prepare an article for publication, they cite works that were of specific relevance to their research. For this reason, the bibliographic references reflect the averaged image of cognitive resources used by the scientists in their work.

The "Science Citation Index" (SCI, United States) is an effective means of investigating citations in science. Each year, there is a separate SCI volume, "Journal Citation Report" (JCR) that summarizes data concerning the articles from periodicals and books cited by authors who published their works in each specific journal. Using the JCR for 1976-1982, we made a comparative study of citations in the periodicals, KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA (KBAM) and AVIATION, SPACE AND ENVIRONMENTAL MEDICINE (ASEM).

For each year, the main or so-called "nuclear" group of citations, which constitutes about 30% of the references, was singled out of the general list of sources cited by contributors to KBAM and ASEM. Apparently, these are the most important sources for researchers. If authors working in the same field in different countries have a similar list of basic sources, it can be considered that they have about the same conception of the subject of their research and use a similar set of basic cognitive means (concepts, theories, methods).

In the Figure, a comparison is made of the structure of citations in KBAM and ASEM in 1982. The structure of citations in the American periodical, ASEM, is shown to the right of the axial line in the form of horizontal bars showing

the relative frequency (percentage) of references to the first most cited basic sources. To the left of the axial line is the diagram showing the structure of references in the array of articles in KBAM. At the bottom of the diagram are listed publications that are among the 15 most frequently cited in KBAM, but not listed among the principal ASEM sources. A comparison of the graphic bars offers an idea about the degree of similarity and differences in structure of citations in the compared periodicals. On the basis of these data one can calculate the parameter of similarity of structure of citations. It equals the share of the overlapping parts of the diagram (if it is mentally folded along the vertical axial line) in relation to its total area. Thus, if we compare the structure of references to 15 sources most frequently cited in 1982, the parameter of similarity between KBAM and ASEM is only 11.3%. This is substantially lower than the corresponding parameters of similarity of structure of citations of other pairs of Soviet and foreign periodicals in the natural sciences that are similar in field. For example, the similarity parameter is 42.3% for the pair of periodicals, FIZIOLOGIYA RASTENIY [Plant Physiology] and PLANT PHYSIOLOGY, 47.9% for the pair VOPROSY ONKOLOGII [Problems of Oncology] and CANCER RESEARCH, 43.1% for the pair ORGANICHESKAYA KHIMIYA [Organic Chemistry] and JOURNAL OF ORGANIC CHEMISTRY.

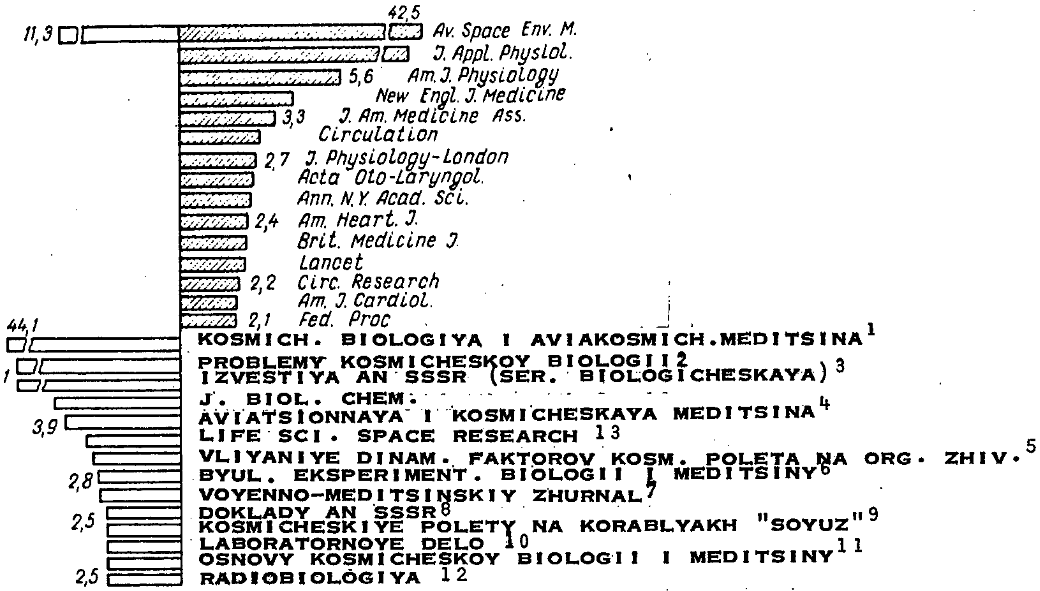
If we were to track the dynamics of this parameter for the periodicals KBAM and ASEM from 1976 to 1982, we would see that it has declined in the most recent time segment. For example, the parameter of similarity of this pair of journals constituted 22.7% in 1976, 19.3% in 1977, 25.2% in 1978, 23.2% in 1979, 21.3% in 1980, 18.4% in 1981 and 11.3% in 1982. In 1982, specialized collections replaced such broad scientific periodicals as FIZIOLOGICHESKIY ZHURNAL SSSR [Physiological Journal of the USSR], AMERICAN JOURNAL OF PHYSIOLOGY and JOURNAL OF APPLIED PHYSIOLOGY, which were contained in the "nuclear group" in 1976.

Table 1.
Indicators of orientation of citations to a field for KBAM and ASEM

Year	Share of specialized editions in file of references to 15 most frequently cited periodicals, %	
	KBAM	ASEM
1976	62,6	38,9
1977	73,0	50,3
1978	72,8	43,6
1979	69,9	44,8
1980	76,2	46,8
1981	69,0	44,6
1982	80,6	42,5
Means	72,0	44,4

Table 2.
Share of citations (%) to works published 10 or more years ago in annual file of periodical articles (for "nuclear group" of sources)

Year	KBAM		ASEM
	Soviet sources	foreign sources	
1976	23,8	47,4	35,9
1977	23,7	56,0	36,2
1978	32,8	70,2	41,5
1979	36,7	57,4	43,1
1980	40,4	50,5	39,8
1981	23,3	59,8	42,7
1982	31,4	55,6	43,8
Means	30,3	56,7	40,4



Comparative structure of citations in KBAM (white bars) and ASEM (striped) in 1982. Horizontal bars show relative frequency of reference (%) to the top 15 most cited publications in relation to total references to them. Right, for ASEM, left, KBAM

Key:

[1]KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA [Space Biology and Aerospace Medicine]

[2]"Problemy kosmicheskoy biologii" [Problems of Space Biology], a series of collections and monographs published by the publishing house, Izdatelstvo "Nauka"; over 50 volumes have been published since 1962

[3]IZVESTIYA AN SSSR (SERIYA BIOLOGICHESKAYA) [News of the USSR Academy of Sciences (Biology Series)]

[4]"Aviatsionnaya i kosmicheskaya meditsina" [Aviation and Space Medicine]; proceedings of 3d All-Union Conference on Aviation and Space Medicine (Kaluga, 10-13 June 1969); edited by Academician V. V. Parin. Vols 1-3, Moscow, 1969

[5]"Vliyaniye dinamicheskikh faktorov kosmicheskogo poleta na organizm zhivotnykh" [Effects of Dynamic Spaceflight Factors on Animals], edited by A. M. Genin, Moscow, Izdatelstvo "Nauka," 1979

[6]BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY [Bulletin of Experimental Biology and Medicine]

[7]VOYENNO-MEDITSINSKIY ZHURNAL [Military Medical Journal]

[8]DOKLADY AN SSSR [Reports of the USSR Academy of Sciences]

[9]"Kosmicheskiye polety na korablyakh 'Soyuz'. Biomeditsinskiye issledovaniya" [Spaceflights Aboard Soyuz Series Craft. Biomedical Investigations], edited by O. G. Gazenko, L. I. Kakurin and A. G. Kuznetsov, Moscow, Izdatelstvo "Nauka," 1976

[10]LABORATORNOYE DELO [Laboratory Record]

[11]"Osnovy kosmicheskoy biologii i meditsiny" [Bases of Space Biology and Medicine], joint Soviet-American publication in 3 volumes, edited by O. G. Gazenko and M. Calvin, Moscow, Izdatelsvto "Nauka," 1975

[12]RADIOBIOLOGIYA [Radiobiology]

[13]Proceedings of periodic COSPAR meetings

The "parameter of orientation of references to a field," which is the share of references to specialized sources of information in the overall file of references to main sources, can also be used. Table 1 lists the values for this parameter for the journals in question over a period of several years (publications were classified as "specialized" on the basis of expert determination). The data in this table indicate that there has been an increase in share of references to specialized sources, and this is more typical of KBAM (from 62.6% in 1976 to 80.6% in 1982).

In addition to the structure of citations, their "age" can also be a rather informative indicator of the cognitive system of scientists [2]. For Soviet periodicals, we list separately the "age" of references to foreign and Soviet sources of information. The share of references to works published 10 or more years ago is their "age."

Unfortunatley, we do not have data concerning the "age" of citations in ASEM referable to sources published in the United States and out of the United States.

Table 2 lists data on the "age" of citations in the periodicals under study.

Table 2 shows that the "age" of citations is noticeably lower in KBAM than ASEM. The only exception are the references to foreign sources in KBAM articles. This is probably attributable to the delay with which the reader receives foreign publications and their relatively poorer availability. In our opinion, the general trend of "aging" of references, which is inherent in both journals but perhaps more to the references to foreign sources in KBAM, merits special attention.

The structure and age of citations are broad diagnostic indicators of the cognitive resources of a scientific discipline in some country or scientific community. Although they are of interest to the management bodies of science and scientists themselves, the conclusions as to positive and negative aspects of some data or other must be drawn with utmost caution, bearing in mind the diversity of factors that determine the status of science.

Our findings enable us to draw the following tentative conclusions.

The structure of citations in KBAM and ASEM is substantially different. The indicator of its similarity is only 10-20%. The structure of citations in both periodicals from 1976 to 1982 presents a tendency toward prevalence of specialized publications, but this is more marked in KBAM. The "age" parameter of citations is somewhat lower in KBAM (with the exception of references to foreign sources) than in ASEM.

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3. Garfield, E., "Citation Indexing--Its Theory and Applications in Science, Technology and Humanities," New York, 1979.

ANNIVERSARY

UDC: 613.693:92 Bryanov

IVAN IVANOVICH BRYANOV (ON HIS 70TH BIRTHDAY)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 3, May-Jun 86 (signed to press 15 Apr 86) p 96

[Article by editorial board]

[Text] Professor Ivan Ivanovich Bryanov, doctor of medical sciences and Honored Physician of RSFSR, has celebrated his 70th birthday.

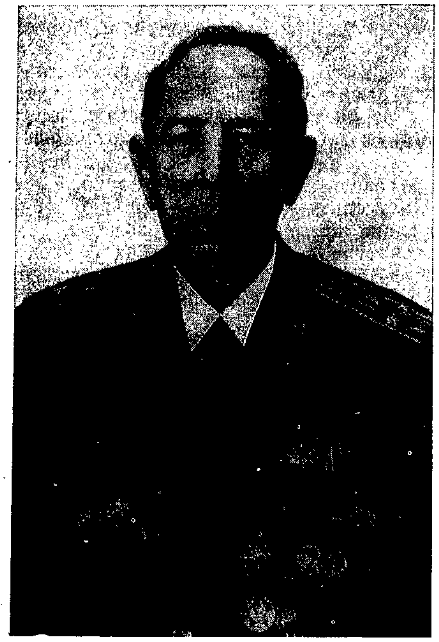
I. I. Bryanov is a well-known otorhinolaryngologist and physiologist, and he is one of the veterans of aviation and space medicine. As an experienced clinician, he developed several valuable methods of examining vestibular functions and criterio for expert medical certification of flight personnel, which are used extensively in medical practice. There has been universal recognition of the contribution made by I. I. Braynov to the study of physiological mechanisms and steps for prevention of space form of motion sickness.

Prof I. I. Bryanov has authored more than 80 scientific works and several inventions. He has done much for the inception and development of aviation and space medicine in the USSR. The Order of the Red Banner of Labor was bestowed upon him for his participation in medical support of the world's first manned spaceflight made by Yu. A. Gagarin. He devoted much effort and energy to medical support of subsequent flights on the Salyut-Soyuz and Soyuz-Apollo programs, screening of Soviet cosmonauts and scientist-cosmonauts from socialist countries (GDR, Polish People's Republic, Hungarian People's Republic).

As a member of the Main Medical Commission, I. I. Bryanov continues his active creative work at the Institute of Biomedical Problems of the USSR Ministry of Health: he participates in ongoing work dealing with medical support of spaceflights; he is chairman of a commission of scientific experts, he oversees dissertation work of his colleagues and reviews scientific publications.

I. I. Bryanov was a participant in the Great Patriotic War and is the recipient of 20 state awards.

All of his coworkers appreciate and have deep respect for I. I. Bryanov as a kind, responsive, wise and fair person, who is principle-minded and exacting in his scientific work.



The editorial board, specialists in aerospace medicine and other allied disciplines cordially congratulate Ivan Ivanovich Bryanov on his birthday, and wish to express their kind wishes for health, happiness and further creative achievements.

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